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TREATMENT OF MENINGOCOCCAL MENINGITIS WITH PENICILLIN*

MANSON MEADS, M.D.,† H. WILLIAM HARRIS, M.D.,‡ BERNARDO A. SAMPER, M.D.,§ AND MAXWELL FINLAND, M.D.¶

WITH THE TECHNICAL ASSISTANCE OF CLARE WILCOX

BOSTON

IN SOME of his early studies on penicillin, Fleming[1] reported that meningococci and gonococci are among the bacteria that are highly sensitive to penicillin in vitro and that they rank with staphylococci in this respect. This observation has been confirmed by others,[2–4] but few strains were tested in each instance. Dawson and his co-workers[5] showed, in addition, that penicillin is effective against experimental Group I meningococcal infection in mice. A total dose of 1800 Oxford units given subcutaneously in sesame oil a half, eighteen and twenty-four hours after intraperitoneal injection of organisms afforded complete protection against 10^{-5} and 10^{-6} dilutions of meningococci, and partial protection against 10^{-3} and 10^{-4} dilutions. These amounts of each of two cultures tested were fatal to control mice in twenty-four hours.

Clinical applications of these findings, as they concern the gonococcus, have been many,[6–12] but they have been chiefly confined to the treatment of sulfonamide-resistant gonorrhea, which almost invariably responds to penicillin in adequate doses. On the other hand, because of the good results obtained with sulfonamides, extremely few cases of meningococcal infections treated with penicillin have been reported. Keefer's[13] series included 5 cases with 1 death. In the fatal case and one other the patient received only parenteral and no intrathecal therapy. Dawson and Hobby[14] reported 2 cases of meningitis; in one, both intrathecal and intramuscular penicillin were given after the patient developed anuria as a result of sulfonamide therapy; in the other, the patient, a seventeen-month-old baby, was given only intramuscular penicillin. The former recovered, and the authors believed that recovery was attributable to the penicillin. The latter made an unsatisfactory response to the penicillin and subsequently responded to antimeningococcus serum and sulfonamide therapy. Both groups of workers concluded that intrathecal as well as parenteral therapy with penicillin is probably necessary to obtain good results. Lyons[15] reported the case of a successfully treated patient with meningococcemia without meningitis who had presumably relapsed after sulfonamide therapy. The War Department[8] recommends penicillin therapy for meningococcal infections only if sulfadiazine cannot be given or if there is a failure to respond to that drug in forty-eight hours. For fulminating cases with bacteremia, collapse and purpura, it is recommended that both penicillin and sulfadiazine be given at the earliest practicable time.

In this paper are presented 9 cases of meningococcal meningitis, including 5 with meningococcemia, that were treated with the calcium salt of penicillin intrathecally and intramuscularly. The reason for presenting such a small series of cases in some detail will become evident from the character of the clinical response that was obtained.

CASES AND METHODS OF STUDY

The cases studied were unselected typical ones of meningococcal meningitis admitted to the Boston City Hospital during April, 1944. The ages ranged from fourteen to fifty-eight years. Seven patients were acutely ill and irrational, 1 was acutely ill and rational, and 1 was only moderately ill when first seen. The duration of the acute illness before entry ranged from one to seven days, averaging about three days. Two of the patients were alcoholic

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

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†Research fellow, Thorndike Memorial Laboratory, Boston City Hospital, and Harvard Medical School.

‡Research fellow, Thorndike Memorial Laboratory, Boston City Hospital.

§Formerly, research fellow, Thorndike Memorial Laboratory, Boston City Hospital, and Harvard Medical School.

¶Assistant professor of medicine, Harvard Medical School; chief, Fourth Medical Service, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital.

addicts, and 4 gave histories of their illness as starting with an acute upper respiratory infection. Blood for sulfonamide determination was taken routinely on admission to ascertain whether therapy with these drugs had been given before entry. No sulfonamide was found except in Case 9, in which the blood level was 2.4 mg. per 100 cc., calculated as free sulfadiazine. It was later learned that this patient had received an oral dose a few hours before entry. Lumbar punctures were done on admission and at twelve-hour to twenty-four-hour intervals, as will be indicated later. Cell counts, smears and cultures of the sediment and chemical studies of the cerebrospinal fluid were carried out routinely. Blood and throat cultures were made on admission and, in some cases, were repeated once or twice daily until they were negative.

Cultures of the spinal-fluid sediment obtained by high-speed centrifugation were made on the surface of 10 per cent horse-blood-agar plates and also in beef infusion broth containing 1 per cent horse blood. Incubation was carried out at 37.5°C. in a candle jar. The time elapsing between lumbar tap and culture was kept as short as possible in order to minimize the penicillin inhibition. In several cases spinal fluid for culture was taken both before and after withdrawing 10 to 15 cc. of fluid, but this did not result in a higher percentage of positive cultures. Identification of the meningococcus was carried out by gram-stained smears of the sediment and by typing. If moderate numbers of gram-negative diplococci were seen, direct typing by capsular swelling[16] was attempted; otherwise, typing was done from the blood-broth culture on the following day.

Treatment

All cases were started on both intramuscular and intraspinal penicillin immediately after the diagnosis was made.

Intraspinal therapy. Initial intraspinal doses consisted of 10,000 to 20,000 units in 10 cc. of sterile physiologic saline solution, to replace a similar or larger volume of spinal fluid withdrawn. The spinal-fluid dynamics were tested before each dose was given to be sure that no block was present. From 5000 to 15,000 units of penicillin was then given intraspinally at twelve-hour intervals for two to five doses and every twenty-four hours after improvement was noted bacteriologically and clinically, and this dosage was continued until clinical and bacteriologic recovery took place. In some cases, the twelve-hour regime was resumed because of the poor clinical response and the persistence or recurrence of abnormal spinal-fluid findings. The number of intraspinal injections given each patient varied from three to eleven, averaging about six, and the total amount of penicillin given intrathecally varied from 30,000 to 150,000 units, averaging about 75,000 units.

Intramuscular therapy. Doses of 15,000 units were given intramuscularly every three hours in 7 cases and doses of 10,000 units every three hours in 2 cases. This therapy was continued until there were signs of definite clinical improvement. The duration of intramuscular therapy was two and a half to six and a half days. The total amount of penicillin given in each case by this route ranged from 190,000 to 1,155,000 units, averaging almost 500,000 units. In Case 7 on the thirteenth day and in Case 8 on the fourth day, because of poor clinical response and persistence of abnormal bacteriologic and spinal-fluid chemical findings, penicillin was discontinued and sulfapyrazine was given, first parenterally and then orally in standard doses. In Case 1, because of persistent positive throat cultures after one week of penicillin therapy, a forty-eight-hour course of sulfadiazine was given orally. No other specific therapy was used.

Results

The relevant findings in the 9 cases are summarized in Table 1 and in the accompanying charts (Figs. 1-7). In all cases except Case 9, a Group I meningococcus was isolated from the spinal-fluid sediment, and in 5 cases the same organism was recovered from blood cultures. In 4 of 7 patients in whom nose and throat cultures were made, a Group I meningococcus was also isolated from the naso-

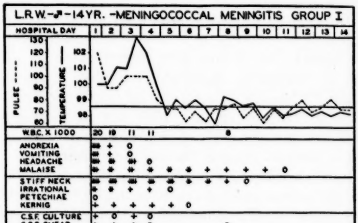

FIGURE 1. *Case 1.*

In this patient the meningeal infection was not controlled bacteriologically or symptomatically until after the fourth day of penicillin therapy. Nasopharyngeal cultures still yielded copious growth of Group I meningococci after a week of intramuscular and intrathecal therapy and after frequent spraying of the nose and throat with a penicillin solution for twenty-four hours. Negative cultures were obtained after one day of oral sulfonamide therapy.

pharynx. One patient (Case 9) who had received a single oral dose of sulfadiazine before entry had negative spinal-fluid and pharyngeal cultures, even though para-aminobenzoic acid had been added to the culture medium.[17]

Clinical Response

In 6 cases, improvement was first observed in one to five days after treatment was started, averaging

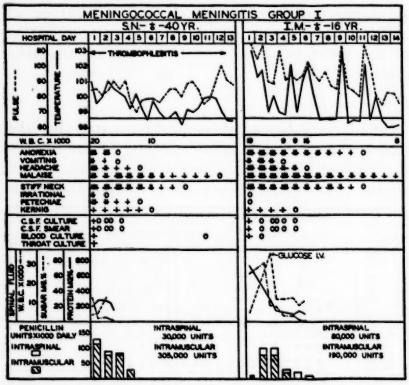

FIGURE 2. *Case 5 (left) and Case 2 (right).*
Each patient showed a prompt bacteriologic response to intramuscular and intrathecal penicillin therapy, but the fever and symptoms persisted for several days.

about three days, as shown in Table 1 and Figures 1 to 5. In Case 7 (Fig. 6) there was a clinical recurrence on the twelfth day, and in Case 8 (Fig. 7) one on the fourth day. The clinical course did not justify continuance of penicillin therapy in these cases and sulfapyrazine was substituted. Response to the sulfonamide therapy was striking and occurred within twelve to thirty-six hours. In Case 9 (Fig. 5), in which sulfonamide therapy had been given before admission, the patient responded favorably after twenty-four hours of penicillin treatment.

The 6 patients treated only with penicillin became afebrile in five to fifteen days, the average being almost ten days. In Case 9, the fever lasted only three and a half days, which was less than in any other case in the series. In Case 7 it continued for only twenty-four hours after sulfonamide therapy was started, and in Case 8 for fifty-two hours.

Bacteriologic Response

Spinal fluid. In 2 of the 8 cases with positive cultures before treatment, the meningococcus could not be cultured at the time of the second lumbar puncture twelve hours after the start of therapy. In 4 cases, cultures of the cerebrospinal fluid remained positive for twenty-four to sixty hours. In Case 7, the culture was positive after twelve hours, and later specimens showed gram-negative diplococci on smear on the fourth and seventh days, along with a recurrence of abnormal chemical findings. Growth in cultures was then obtained on the twelfth and thirteenth days. In Case 8, the last time growth of meningococci was obtained was after twelve hours, but positive smears were found after ninety hours.

Blood. In all 5 patients with positive blood cultures on admission, all subsequent cultures were negative. The second blood culture was always taken ten to twelve hours after the start of therapy.

Throat. Repeated throat cultures were made in 2 of the patients whose initial cultures were positive. The last positive culture in one of them (Case 8) was obtained after three days, and in the other (Case 1) after seven and a half days of intramuscular penicillin (660,000 units). In the latter, the culture was still positive after twenty-four hours of throat and nose spray with penicillin (400 units per cubic centimeter every two hours during the day and three times at night). In both the patients, the throat cultures became negative for meningococci within forty-eight hours after sulfadiazine was given orally in therapeutic doses.

Clinical and Cytologic Response of Spinal Fluid

As evaluated by the protein and sugar levels and the number of cells and their differential count,

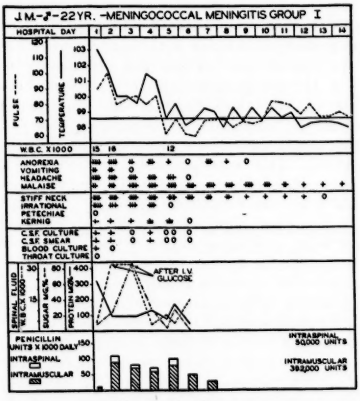

FIGURE 3. *Case 3.*
Cultures of the cerebrospinal fluid in this patient did not become negative until the fifth day of intramuscular and intraspinal penicillin therapy. During that time the patient continued to be irrational; he improved slowly thereafter.

the spinal-fluid findings returned approximately to normal in two and a half to eight days, with an average of five and a half days.

Complications

No complications occurred that could be attributed to the calcium salt of penicillin except possibly a scarlatiniform rash that appeared in 1 case on the fourth day of penicillin therapy. It is possible, however, that this rash was a result of erythro-

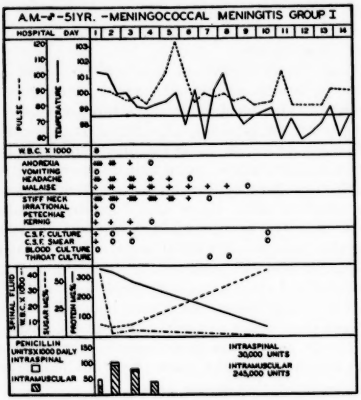

FIGURE 4. *Case 4.*

In this case, cultures of the spinal fluid were still positive on the third day. The patient was definitely improved after twenty-four hours but continued to have some meningeal symptoms for several days.

toxins derived from extensive herpes lesions that were secondarily infected with *Staphylococcus aureus* at the time of onset of the rash. In Case 5, there was a thrombophlebitis on entry, which became worse on the third hospital day and persisted through the twelfth day. One patient (Case 6) had a convulsion eight hours after the first intrathecal injection. This was probably due to increased cerebrospinal-fluid pressure, which may have resulted from the penicillin injection.[18] In Case 7, there developed signs of consolidation of the left lower lobe, and many Type 8 pneumococci were identified in the sputum thirty-six hours after the intramuscular penicillin therapy was stopped. This complication failed to respond clinically or bacteriologically to doses of 15,000 units of penicillin given intramuscularly every three hours for forty-eight hours. One patient (Case 9) developed arthritis of the right knee on the third hospital day; on the ninth day, this was tapped and culture of the fluid was sterile.

Tests for Sensitivity of Strains

The strains of meningococcus recovered from 5 patients in the present series were tested for sensitivity to penicillin according to the method used by Rammelkamp and Maxon.[19] One strain was completely inhibited by 1.25 units per cubic centimeter, 3 by 0.625 units, and 1 by 0.312 units. The latter was obtained from Case 1, and the organism obtained after one week of penicillin therapy in this case was also tested and showed no increase in its resistance. This range of sensitivity puts these particular strains in a category with the more resistant strains of *Staph. aureus* and *Streptococcus viridans*.

All five strains failed to grow in peptone-free synthetic media containing 1 mg. per 100 cc. of sulfadiazine. This may be taken as an indication of the great sensitivity of these strains to sulfadiazine in vitro.

Penicillin Levels

Spinal-fluid levels of penicillin, tested by the Rammelkamp and Maxon[19] method of serial dilution against a stock strain of streptococcus, varied within wide limits. They showed that the levels

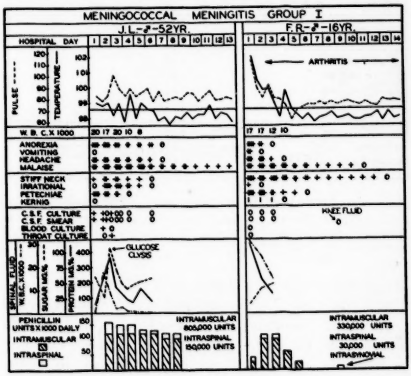

FIGURE 5. *Case 6 (left) and Case 9 (right).*

In Case 6 the patient continued to have positive blood cultures (Group I meningococci) for twelve hours and positive spinal-fluid cultures for thirty-six hours after intensive intramuscular and intrathecal penicillin therapy. He remained acutely ill for about five days, after which he steadily improved. In Case 9, the clinical features were characteristic of cerebrospinal fever but all cultures and smears taken on admission were negative for meningococci. It was later learned that this patient had received a single dose (2 gm.) of sulfadiazine shortly before being sent to the hospital, and blood taken on admission showed a free sulfadiazine level of 2.4 mg. per 100 cc. Definite clinical improvement occurred within twelve hours and continued steadily thereafter.

obtained in the lumbar canal eight to twelve hours after intraspinal injections were more than adequate for bacteriostasis.

COMMENT

Smith et al.[20] reported 43 cases of meningococcal meningitis treated with sulfonamides. Twenty were Group I infections, and 5 of these patients died. In 14 cases in which the clinical response could be

evaluated, the average time between the initial dose of sulfonamide and clinical improvement was one day. Fever persisted for an average of five and a half days after the onset of treatment. In 11 cases, negative cerebrospinal-fluid cultures were

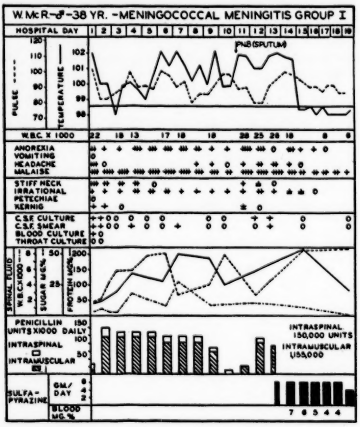

FIGURE 6. *Case 7.*

In this patient the infection was not controlled clinically or bacteriologically after nine days of intensive intrathecal and intramuscular penicillin therapy. On the second day after intramuscular injections were discontinued, the patient developed lobar pneumonia of the left lower lobe and a copious growth of Type 8 pneumococci was obtained from the sputum. Resumption of penicillin therapy failed to control either the meningeal or the pulmonary infection. Clinical improvement began within a few hours after sulfonamide therapy was started, and the patient had essentially recovered thirty-six hours later.

obtained twelve to eighteen hours after the start of therapy and in the remaining 3 the cultures were positive for seventeen to twenty-four hours. Banks[21] in a series of 72 cases treated with sulfanilamide and M. & B. 693 without antiserum noted that the acute symptoms disappeared rapidly and the temperature in most cases returned to normal in two to six days. In 66 patients the spinal fluid was sterile in twelve to twenty-four hours and in 4 it became sterile in twenty-four to forty-eight hours; only 1 patient was found to have a positive fluid after forty-eight hours. Spinal-fluid cell counts fell to below 500 in three or four days, and 90 per cent of the cells were mononuclears in five to six days.

The efficacy of the sulfonamides has been shown in a review of mortality rates by Dingle and Finland.[22] In over 1000 cases treated with sulfanilamide there was a mortality rate of 14 per cent; in 700 cases treated with sulfapyridine and 26 treated with sulfathiazole it was 8 per cent. Recently, in a series of 129 sulfadiazine-treated cases of meningococcal meningitis, Marangoni and D'Agati[23] reported a mortality of 3.1 per cent, and Appelbaum and Nelson[24] reported a 1.4 per cent mortality in 141 consecutive cases treated with sulfadiazine and its sodium salt.

The results in the 8 cases reported here in which no sulfonamide therapy had been given previous to admission show clearly the poor clinical and bacteriologic response to calcium penicillin obtained in cases of Group I meningococcus meningitis as compared with sulfonamide-treated cases. In this series, it is impossible to evaluate the effect of the intraspinal therapy in relation to the severity of infection on admission and to the duration of illness before treatment. From bacteriologic sensitivity tests and from observed spinal-fluid penicillin levels, it can be assumed that many more times the bacteriostatic level of penicillin was obtained for at least twelve hours after its installation in the lumbar canal. The most probable explanation offered at present is, first, the failure of penicillin to penetrate to any significant extent into the cerebrospinal fluid from intramuscular or intravenous administration, and second, the failure to obtain a proper distribution of penicillin throughout the cerebrospinal fluid after intraspinal injection, thus preventing contact of the drug with many of the organisms. This may serve to explain the per-

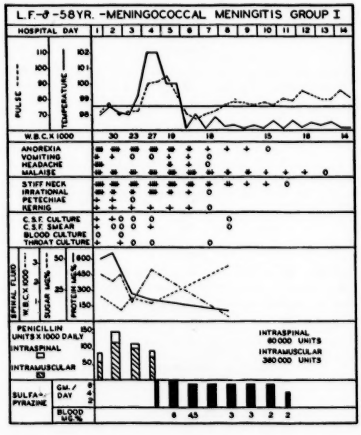

FIGURE 7. *Case 8.*

This patient remained acutely ill and irrational during four days of therapy with penicillin intrathecally and intramuscularly. Because he was obviously getting worse clinically, sulfonamide therapy was then given. Improvement began within a few hours and steadily continued.

sistence of exudate and consequent pocketing-off of organisms, adhesion formation and pressure difficulties. The rapid and complete distribution of the

sulfonamides throughout the cerebrospinal fluid results in early resolution of exudate, as shown by post-mortem studies. This may explain the much more favorable clinical and bacteriologic response to the sulfonamides.

In these patients the number of lumbar punctures in each case varied from three to eleven. An average of six taps were done in addition to occasional unsuccessful ones. This factor makes management difficult as compared with sulfonamide administration, in which often a single diagnostic puncture is all that is necessary.

Meningococcemia, on the other hand, seemed to respond rapidly. The persistence of positive throat

TABLE 1. *Summary of Clinical and Bacteriologic Findings in Nine Cases of Meningococcal Meningitis Treated with Calcium Penicillin.*

Case No.	Age	Sex	Duration at Entry	Predisposing Factors	Severity at Entry*	Initial Bacteriologic Findings†				Penicillin Treatment						
						Cerebrospinal Fluid		Blood Culture	Throat Culture	Intramuscular			Intraspinal			
						Culture	Smear			3-hour Dose	Duration	Total Dosage	Single Dose	Interval	No. of Doses	Total Dosage
	yr.		days							units × 10³	days	units × 10³	units × 10³	hr.		units × 10³
1	14	M	2-3	Upper respiratory infection (3-4 days)	+++	+	+	0	+	15 10	6 1½	660	15 10 15 15	12 24 24 120	2 1 1 1	70
2	16	F	1½	0	++	+	+	+	−	10	2¼	190	10 10 10	12 24 12	4 2 2	80
3	22	M	3	0	+++	+	+	+	0	10	5½	392	10 10 10	12 24 12	3 1 2	60
4	51	M	2	Upper respiratory infection 7 days; chronic alcoholism	+++	+	+	0	−	15 10	½ 2	245	15 10 5	Stat. 12 24	1 1 1	30
5	40	F	3	Upper respiratory infection (7 days)	+++	+	+	+	+	15 10	½ 2½	305	10 5 5	Stat. 12 24	1 3 1	30
6	52	M	1	0	+	+	+	+	+	15	6½	805	20 15 15 10 15	Stat. 12 24 24 24	1 5 1 1 2	150
7	38	M	7	Chronic alcoholism	+++	+	+	+	0	15 0 15	7½ 4 2	1,155	15 15 10 10 10	12 24 36 24 36	4 4 1 1 1	150
8	58	M	3	0	+++	+	+	0	+	15	3	360	15 10 10 15	Stat. 12 24 24	1 2 1 1	60
9	16	M	2	Upper respiratory infection (7 days)	+++	0	0	0	0	15 10	2 1	330	10 10	12 24	2 1	30

*+++=acutely ill, irrational; ++=acutely ill, rational; and +=moderately ill.

cultures in one case for four days and in another until sulfadiazine was given on the ninth day reveals another possible disadvantage of penicillin therapy. fections. Cheever et al.[25] in a study of 161 cases of meningococcal infections of the nasopharynx showed that nasopharyngeal cultures became negative for

TABLE 1 (*Continued*).

CASE No.	RESPONSE TO PENICILLIN THERAPY						COMMENTS, COMPLICATIONS AND SO FORTH
	BACTERIOLOGIC†				CLINICAL‡		
	Cerebrospinal Fluid Culture	Fluid Smear	Blood Culture	Throat Culture	Definite Improvement *days*	Afebrile *days*	
1	38 hr. 62 hr.	38 hr. 62 hr.	0	9 days 10 days	5	9	Penicillin by nose and throat spray for 24 hr. on 8th day; sulfadiazine from 9th to 11th day.
2	Admission 12 hr.	Admission 12 hr.	Admission 12 hr.	—	4	12	
3	60 hr. 84 hr.	60 hr. 84 hr.	Admission 12 hr.	0	5	11	Extreme weakness; clinical and bacteriologic recurrence on 4th day.
4	40 hr. 9 days	Admission 12 hr.	0	—	1	9	Scarlatinal rash from 4th to 8th day.
5	Admission 12 hr.	Admission 12 hr.	Admission 12 hr.	—	1	15	Thrombophlebitis on entry; patient worse on 3rd day; improved on 12th day.
6	24 hr. 36 hr.	12 hr. 18 hr.	Admission 12 hr.	12 hr.	4	5	Convulsion 8 hr. after first lumbar tap; patient looked worse and remained confused for 3 days in spite of improved spinal-fluid findings.
7	13 days 15 days	13 days 15 days	Admission 10 hr.	0	14	14	Lobar pneumonia (Type 8 pneumococcus) on 11th day — 36 hr. after intramuscular penicillin stopped; three apparent clinical and bacteriologic relapses under penicillin therapy; complete recovery after sulfapyrazine in 36 hr.
8	12 hr. 24 hr.	4 days 8 days	0	2 days 3 days	5	5	Patient given sulfapyrazine on 4th day because of increasing irrationality and no improvement in spinal-fluid findings; response to sulfapyrazine in 12 hr.; serologic syphilis (blood and spinal fluid).
9			0		½	3½	Arthritis in right knee 36 hr. after entry (first tap, on 9th day, sterile); blood sulfadiazine on admission 2.4 mg. per 100 cc. (patient had received one oral dose 2 to 3 hr. before entry).

†The numerator indicates time (at or after admission) of last positive culture, and the denominator the time of the first subsequent negative culture; 0 indicates that all cultures were negative, and — that no cultures were taken.

‡The intervals represent the time after the first dose of penicillin.

Adequate bacteriostatic levels of penicillin probably did not reach the nasopharynx in these cases. This certainly is another important consideration favoring the use of sulfonamides in meningococcal in- meningococcus in all cases within seventy-two hours after a dose of 8 gm of sulfadiazine. This has now been adequately confirmed, even with smaller doses.[26, 27]

The possibility that the calcium penicillin used in the present cases was inferior in its therapeutic effects was considered. This seems unlikely for the following reasons. In vitro tests indicated full activity, in Oxford units, against standard strains of other bacteria. The same batch of calcium penicillin was given at the same time to a much larger number of patients with various other diseases, including cases of pneumococcal meningitis, with results comparable to those obtained with similar amounts of sodium penicillin. Intrathecal injection of the same lot in other subjects gave reactions that were actually slighter than those obtained with similar amounts of sodium penicillin. There were no local reactions from its use intramuscularly.

If good results are obtained from the treatment of meningococcal meningitis with penicillin, one must suspect that the patient has received sulfonamides before entry. He is not always in a condition to give a history of such therapy. The potent bacteriostatic effect of these drugs on the meningococcus is such that even one or two small oral doses may suffice to produce a complete bacteriologic and clinical response, as indicated by the experiences in the Anglo-Egyptian Sudan in 1938.[28, 29] This was probably the factor that contributed to the rapid and favorable response observed in Case 9.

A comparison of the results of therapeutic studies on meningococcal infections in mice lends further support to the greater effectiveness of sulfadiazine *in vivo*. Thus, in contrast to the 1800 Oxford units used by Dawson et al.,[5] as mentioned at the beginning of this paper, Thomas and Dingle[30] protected mice against similar infections with ten to ten thousand times the 50 per cent lethal dose of a virulent Group I meningococcus by giving only a single dose of 0.0025 mg. of sulfadiazine. For the average adult patient, these doses are equivalent, weight for weight, to about 10 mg. of sulfadiazine and 7,200,000 units of penicillin. The two studies are not entirely comparable, but the figures are certainly impressive when considered together.

Lastly, the finding in five consecutive cases of strains of meningococcus that are relatively resistant to penicillin seems to be in marked contrast to the results reported by others. Great differences in susceptibility to penicillin must occur and should be further investigated. These findings may explain, in part, the poor results obtained in this series.

Conclusions

The clinical and laboratory findings in this series of 9 cases of meningococcal meningitis treated with calcium penicillin, when viewed in the light of the accumulated results of sulfonamide therapy, suggest that the sulfonamides are the drugs of choice in the treatment of Group I meningococcus meningitis, and that penicillin may be effective in Group I meningococcus meningitis in the doses used, but that the response is less favorable than that from sulfonamide therapy.

If penicillin is used, careful observations should be made of the clinical course, the spinal-fluid and nasopharyngeal bacteriology and the spinal-fluid chemistry.

The clinical response to penicillin is slower than that to the sulfonamides; abnormal spinal-fluid chemical and bacteriological findings persist longer; there may be recurrences; the meningococcus-carrier state may persist; the treatment is difficult; and, finally, one may eventually have to resort to the sulfonamides for cure.

Calcium penicillin seems to be quite effective against Group I meningococcus bacteremia.

Strains of Group I meningococcus vary markedly in their susceptibility to penicillin. In this respect, the strains studied in the present series resembled the relatively resistant ones of *Staphylococcus aureus* and *Streptococcus viridans*.

Several significant papers bearing on the present subject have appeared since this one went to press. Miller and Foster[31, 32] reported favorable responses in vitro and in experimental infections with meningococcus, but special methods were required for this purpose. Rosenberg and Arling[33] used sodium penicillin in the treatment of 71 cases of meningococcal meningitis and meningococcemia without meningitis and noted favorable clinical responses, but many of the bacteriologic responses were similar to those reported here. Their general method of treatment was similar to that used in this series except that more thorough drainage of the spinal fluid was done before each intrathecal injection of penicillin. The authors, however, do not mention how frequently sulfonamides were used in their cases, and no mention is made of any special effort to determine that point. Only in the single fatal case is it noted that the patient received both sodium sulfadiazine and penicillin. From observations in our clinic and from many reports in the literature, particularly the experience in the Sudan,[28, 29] it is to be expected that a single dose (2 or 4 gm.) of a sulfonamide given by a medical officer in a dispensary at the time when the diagnosis is suspected would be adequate to bring about most of the beneficial results. Rosenberg and Sylvester[34] were able to recover penicillin from the spinal fluids of cases of meningitis in concentrations of 0.03 to 0.35 unit per cubic centimeter after intravenous or intramuscular injections of 20,000 to 40,000 units. If this is corroborated it may prove possible and desirable to eliminate intrathecal therapy in some cases of meningitis and thus to avoid one of the major objections to the use of penicillin in these cases. Actual experience in treatment of cases of meningitis with penicillin alone would not seem to bear out this expectation.

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ARE DOCTORS PEOPLE?*

ROGER I. LEE, M.D.

BOSTON

IN MANY of the folklores, the doctor, or rather his analogue or prototype, appears as being quite set apart from ordinary people. He is seen in many forms and guises. If there is a touch of the lower animal about the medicine man, there is more of the deity. There is more of the saint than the devil, but some of both. There is madness, witchcraft and chicanery, but there is a larger amount of wisdom, sanity and honesty.

Of course primitive people merely created out of their own composite experiences — emotions, desires, fears and joys — their own gods, devils, saints, medicine men and various other important figures in their daily lives. Once the pattern was roughly established, there was a strong tendency to continue the type. But each medicine man used his own imagination, his own personality, good or bad, his own experience and a few of his own tricks to alter the pattern somewhat.

Strong members of the community or tribe always attempted to use the medicine man for their selfish ends. Sometimes they succeeded, sometimes they lost, and sometimes there was a new medicine man. Likewise, strong men would find that at times the gods were wholly co-operative, as we may call it. If there were priests of one kind or another who divulged the pleasure or displeasure of the gods, the priests might be persuaded to make a somewhat different interpretation, or possibly the strong men might do their own interpreting and find it easier to head both the spiritual and the temporal organizations. This was rarely done in the case of the chieftain and medicine man, but the union of the priest and medicine man sometimes happened.

No brew of medicine, however, no matter how cunningly concocted, even in the most favorable phase of the moon, or even if subjected to the loudest of incantations, can heal certain mortal wounds or cure certain mortal diseases. Nor can such a brew restore a lost limb, eyesight or hearing. Nor can it replenish the ravages of time, more particularly in those feats of prowess fostered by the gods and goddesses of war and love. Thus it often seemed the part of discretion, if not of wisdom, to leave the medicine man, so to speak, on his own. If his brews, medicines and incantations were not satisfactory, one could try the potions and performances of another medicine man, perhaps one in a near-by community, perhaps one in a distant community, who had a reputation for healing certain ailments, or perhaps an upstart competitor in the same community.

Well, has the situation changed very much fundamentally? Patients get dissatisfied and seek help in distant places now as they did in the days of medicine men, perhaps as far from Worcester as Boston, New York or Rochester, Minnesota.

The community gets about the sort of medical practice it really wants and creates. At times the doctor is better than the community deserves, but in a small community especially, the medicine man of old and the doctor of today are quite at the mercy of malicious gossip. Of course, it is true that whereas the doctor gets blamed for many circumstances and accidents over which he has no control, he is also praised for certain happy outcomes to

*An address given by the president of the Massachusetts Medical Society at the one hundred and fiftieth anniversary of the Worcester District Medical Society, Worcester, May 10, 1944.

which he contributed nothing — even though the balance is favorable to the doctor. Such a situation is stupid and wholly harmful. In the more recent but still bygone days of the apprentice method of education of the doctor, the old doctor passed on to his apprentice the secrets and tricks of his practice. Those were the days of rugged individualism of the doctors. It was this type of family doctor who caught the imagination and acquired the affection of a grateful community. Perhaps his practice of medicine was not perfect. Perhaps only sometimes did he bring cure, but he always brought comfort, physical and mental, to the patient and his family. In the modern days of formal medical education, medicine is far, far better, but it is not now free and independent. It is less so than in the days of the family doctor. Unfortunately or fortunately, as you will, medicine is now under the profound influence of lay opinion and lay action. The controlling bodies of educational institutions are naturally largely composed of laymen, that is, so far as medicine is concerned. Furthermore, there is a further lay and, at times, political control of the funds of some of the state medical schools. Of course the situation varies, but the president of a state university has to spend much time defending his budget before legislative committees. Some of these legislators have extremely positive ideas in regard to education, including medical education. The rejoinder is obvious, namely, that the president of a privately endowed university spends his time in argument with possible benefactors instead of with state legislators; and benefactors, like legislators, have their prejudices. In other words, the community still creates the medicine man in the image and in the pattern that it conceives to be the kind that delivers the most effective brew.

Now, this concept is not entirely whimsical, because it was not so long ago that a health officer found himself in jail for having ventured to diagnose a case of bubonic plague. That part of the country would not admit the existence of plague, and that was that. Of course the disease was not plague, and the doctor got out of jail, but after all, it was a lay resort to coercion in an unpleasant dilemma. It was merely the old story in a new setting: the tribal chief was sterile and his favorite wife was pregnant. Medical truth in the early days bowed to social convention, and today sometimes has to give a nod if not to turn a deaf ear.

Leprosy is a terrible disease, and no one wants to catch it. Consequently, because you and I do not want to have it, in our lay capacities we permit the unfortunate victims of this disease to be segregated on lonely islands. Such is the law and the practice. The truth is that leprosy is not especially contagious. Such barbaric cruelty is unjustified by the known medical facts.

These illustrations could be multiplied many times, merely adding more evidence of the dominance of the community over the medicine man. But it is not solely the dominance and control of medicine by the community that I want to discuss. We must accept the fact that the community, from the days of folklore and the medicine man to the present, conceives the medicine man and the doctor as someone apart from the rest of the tribe or the rest of the community. In the old days the medicine man often lived apart, painted his face egregiously and wore extraordinary masks. As a part of his performance he went through grotesque gyrations and gymnastics. Within the memory of many listeners, doctors wore an affair called a "Prince Albert" or frock coat. Certainly doctors were then, even more than now, rugged individualists, and I cannot visualize a convention of doctors setting up the Prince Albert coat as a sort of uniform for the profession. Consciously or not, the wearing of it was a dictum from the community. And take the gold-headed cane of another era. I have always maintained that the only practical use of the gold head was for the physician in those days to thrust it into his mouth to prevent his making any more of an ass of himself than he had already.

An erstwhile intern of mine in another city replied to my remark that because he drove such a luxurious car he could not be doing so badly financially. "In this city, patients will not go to a doctor who drives a Ford. I know because I tried it, and all my good friends and good patients spoke to me about it." I was about to make some remark more emphatic than polite about that city and state when it occurred to me that I had intended to ask him how he liked his office in an office building, since I was considering moving my office to a similar building in Boston. Such a building had, at first anyway, to be within a very restricted area — just the opposite of course, to the red-light district in character but really having the same implications. Of course, if one is famous like the Mayos, it makes no difference where one's office is. I know a doctor who receives his patients in bathing suits on the sand under a sun umbrella, but the locality is Palm Beach, and the doctor is a neuropsychiatrist.

Not long ago, a United States senator telegraphed that twenty doctors were needed at once for a war-boom town in his state. By the time the "sob sisters" in New York City got through with the story, it was two hundred doctors. There was no information about the kind of doctor wanted. It turned out that probably two doctors were required for a manufacturing plant — one a general practitioner and the other a physician with some knowledge of industrial medicine. The plant had been running for several months, and although its operator had not forgotten about his contract,

his site, his men or his materials, he had forgotten the doctor.

One is always hearing of large areas without a doctor. I have traveled through some of those large areas, and there appeared to be little worth while in them, except the train I was riding in. Whole counties in Kentucky do not have a doctor. I used to be dismayed by this until I learned how many counties there are in Kentucky. I have forgotten the number, but it is well up in three figures. What kind of doctor do people want in the mountains of Kentucky and Tennessee? Certainly not a "damn Yankee" doctor. He would not get a chance to practice. A native doctor could practice, but he could not be paid because there is nothing to pay him with. Incidentally, there is no provision in the Wagner–Murray–Dingell Bill that includes these people; it provides only for industrial people, for whom it is compulsory.

As one goes through Massachusetts one finds small settlements, often a so-called "village," without any doctor. One looks at the deserted mills, the deserted farms. One hears someone say, "Most of the people have left, but you'd think some doctor would come." Are doctors people?

Years ago I was on a committee that attempted to study the distribution of doctors, especially in rural communities. We tried to collect cases of hardship, lack of care and forced neglect, but could find only one such case. The complainant was a farmer who testified that on such and such a day he tried to get a doctor to come to see his wife but the doctor would not come. It was in the winter and in the night. His wife had been sick for a couple of weeks but was in "great pain." Somehow or other she got over her illness, but it was terrible, and we were told "Doctors ought not to be allowed to get away with things like that." So we got hold of Doctor Blank. He knew this farmer and occasionally treated him or some member of his family. He had a general idea of where the farmer lived. He was at first rather puzzled by the tale, but finally said:

> I'm sure this is the story, but you had better check it with the farmer. It was midwinter and snow was falling. I had just gotten in from a confinement case. After a telephone argument over how sick the wife was, I finally said I'd come, that I would follow the plow the next trip to such and such a corner where the farmer would meet me with a horse and sleigh. That was a common arrangement. However, the farmer said, "Go out on a night like this? I would not send a dog out." Whereupon I hung up.

Subsequently, the farmer verified the complete story, adding that he was tired. To the remark that the doctor might be tired too, he merely replied, "Oh, they get used to it, and if they can't, they ought to do something else."

Now, the Christian Scientist decidedly poohpoohs some of the material things in life, but the "reader" is sound and safe in situations like the foregoing, because he or she gives the patient absent treatment and does not have to go out in the blizzard of a winter's night.

Just now the armed forces want doctors, physically active ones, for our boys, and the war industries want industrial doctors, while the good folks at home get along courageously with self-rationed medical advice and treatment.

There seems to me to be much too much talk that a doctor is demanded here or there, on this mountain or at this village corner. If doctors were turned out on assembly lines in mass production, it might make sense to talk of so many here and so many there. Of course, the product would be mechanized. What is wanted are good doctors, skilled doctors, not by any means always specialists, but "regular-guy" doctors.

Doctors are human beings notwithstanding the fact they are not supposed to be tired, to have vacations or to enjoy uninterrupted dinners or golf games. For months, on the front pages of most daily newspapers, appeared statements of how soon the draft would begin to take fathers. Senators and representatives in Congress announced that they would fight — in Washington, D. C., not in uniform — to the last ditch the drafting of fathers. Doctors, being ordinary people, seek to marry beautiful and intelligent girls. Doctors' wives have seen their husbands volunteer, even before Pearl Harbor, and leave their homes and children. Many of them have been over thirty-eight and even over forty-five. But doctors were not supposed to object. Since the good women are also human, they sometimes object, but the doctor goes. When the war is over, he will not come back to that salary and that pension, but will be obliged to build up his practice all over again in a world that believes that it created doctors in a certain pattern and therefore can destroy them.

After the war, history will tell of great medical discoveries in it. Plasma and penicillin will be cited. There cannot be found better illustrations of lay domination of medicine. To all intents and purposes, plasma and the theory of plasma was "frozen" — to use the modern jargon — from the end of World War I to the beginning of World War II. Twenty years after World War I, medical scientists continued working as if those twenty years had not existed. The story of penicillin is more picturesque. In 1928, Professor Alexander Fleming, of London, made the observation that germs would not grow with or close to the colony of a common mold. Doubtless other men had observed the same thing, but Fleming puzzled over it and finally published this observation. Years went by and nothing happened. Fleming once showed this phenomenon to me, as he did to many others. Certainly something ought to have been done about it. It was only the threat of war and war itself that furnished the impetus that has produced penicillin. You would

not believe, if I told you, the number of millions of dollars poured into the development of penicillin. It is a new agent in combating infections. It may be that we shall be disappointed in the final place of penicillin, but its present promise dazzles the imagination. And yet without the war no man can ever know whether penicillin would have been developed or how many years it would have taken to develop it. Once again, I must point out to you that the doctors are not the masters of medicine or medical practice, even today.

Certainly the legislature of Massachusetts years ago inflicted a terrible medical practice act on this state, and for years the sovereign Commonwealth of Massachusetts has been the dumping ground for incompetent doctors who were not allowed to take or could not pass the examinations in any other state. Finally the stench reached the Legislature, which recently framed a good bill. But it took a courageous minority of the Board of Registration in Medicine, including fine Dr. Atwood, of Worcester, and a courageous governor to complete the cleansing process of the Augean stables. But what of the hundreds of incompetents who *bought* their licenses to practice medicine in Massachusetts? Thus, it is not the good doctors who determine the standards of medical practice but the community itself. It perhaps creates the doctor in its own image, which can be evil.

It has been to the everlasting credit of the medical profession of this country that traditionally doctors do not patent their discoveries. Recently there has been some wabbling in this attitude. Curiously enough, some medical schools have sought to profit — and some of them have done so mightily — by taking over the patents and the royalties therefrom. The story is told of the opening of the new Harvard Medical School about 1905. A famous New York banker had been a very generous benefactor, but universities are always venal and grasping. The university's star beggar took the New York banker around. The beauties of the buildings were appropriately described. The young scientists were likewise duly noted. "Alas!" said the beggar, "If only we had a little more money to put these trained young men to work." "Humph!" said the banker, "If you have the space and the bright young men, why don't you have one of them invent a good patent medicine? That gives bigger returns than anything I know."

I should like to talk at great length on medical patents and their iniquities, but God be praised, an important court has held a patent that benefited one medical school as invalid, and President Robert Hutchins, of the University of Chicago, has come into the fold of patent purity in medicine. When I am finally sure that any scientist can work with scarlet fever, its germs, its toxins, its antitoxins and its antiserums without a special license from the University of Chicago committee on whatever they call it, I shall write President Hutchins a nice letter congratulating him on seeing the light. But, mind you, this only illustrates the possibilities of lay domination of medical science in accordance, no doubt, with the best Christian practices in business, but leaving the medical men merely puppets.

Now, God forbid that doctors should organize a union, even if that action exempted them from the operation of the anti-trust laws. We do not want any Little Steel Formula. There is too strong a possibility that the other fellow might have a different spelling of "steel."

As I have tried to point out, the lay domination of medicine has been going on since the beginning of time. The medical profession has at times approached independence but it has never been free, certainly not in the way that the profession of law has been independent and free, and master of itself.

Over the years since the turn of the century, there has developed a trend, not new, but for the first time really powerful, that represents a new social philosophy. It came into full flower when social sciences were reorganized as a separate sector of human experience and human knowledge. The enthusiasts of this school of thought lump more or less all the human miseries together. Whereas the doctor looks at his patient through a microscope, the social scientists look at illness through a telescope. Perhaps Sir William Beveridge can be regarded as one of the most articulate, most logical and most reasonable of the exponents of this new social philosophy. He has five giants that must be overcome on the way to "reconstruction," as he calls it — "millennium" is my humble contribution in words. These giants are Disease, Idleness, Ignorance, Poverty and Want. There are other thinkers, perhaps on the outskirts of this philosophic trend, who would mention Superstition, Prejudice, Selfishness and Greed. Within the fold of this cult, however, poverty is the mother of disease. The paternity of disease is usually left obscure. These social scientists would therefore take over disease — the study of disease, the prevention of disease and the treatment of disease — and make themselves masters of medicine and the medical profession. Now, lest you think I am entirely mad, I hasten to add that this, I find, is a favorite theme of a Jesuit priest, Father Schwitalla, who happens to be dean of the St. Louis University School of Medicine, and president of the Catholic Hospital Association of the United States and Canada.

Some years ago I found Professor George Foot Moore, perhaps then Harvard's greatest scholar, in something that in anyone else than a professor and an ordained minister would be called a rage. He had been examining students for the degree of doctor of philosophy. A colleague gave the student a somewhat lengthy case history, which Professor

Moore said was the story of a bum, a very ordinary bum. The student candidate was asked for his social diagnosis. When the student answered, "Frustrated childhood in an environment of poverty," Professor Moore exploded. Doubtless there are frustrations, doubtless there is poverty. But I agree with Professor Moore that there are also probably bums, and with Prime Minister Winston Churchill that there are also pub crawlers.

In any event, the social scientist would put disease and the medical profession within the Social Security Act, with a social scientist in the Cabinet. As is evidenced by the Wagner–Murray–Dingell Bill, the problem is regarded as economic. Curiously enough, what they want to toss at this hungry, poverty-stricken and diseased wretch is medical service. Now, most doctors would like, so far as possible, to separate the economic and medical aspects. So far as I know, no substantial group of doctors is opposed to the control and relief of poverty, unemployment and the distress of old age, and in the control and relief of poverty doctors would include shelter, warmth, food and the like. And certainly doctors want to have not a better but the best distribution of medical care or "medical service" if you like the new jargon. To the doctor human beings are living entities, not case numbers on a blueprint. Likewise a doctor is a human entity. He is no blue-headed pin to be stuck on a map to take care of so many red-headed pins representing patients.

We all know that in some respects mechanized medicine will work fairly well. You can take the urine of a woman down to the laboratory, and some little laboratory animal will whisper to you whether the woman is pregnant or not. But, for heaven's sake, be careful not to get the bottles mixed. And the impersonal laboratory said authoritatively that Charlie Chaplin was not the father of a certain child. But the mechanization of medicine can be carried too far, and it will be if this present trend continues.

Doctors seem always to have been dominated by others and never to have been complete masters of themselves and of their profession. It seems that this present trend of social, economic and political philosophy threatens them with more dominance than they have ever known. Although I believe this to be a menace to the grandest profession in the world, who am I to venture upon prophecy?

Please note the humility and the altruism of the doctors of Worcester who founded this society one hundred and fifty years ago. This was a collection of men who planned not to aggrandize themselves but rather to improve themselves, and thereby to benefit the whole community.

Of the same temper are the words in the charter of the Massachusetts Medical Society and that of the American Medical Association. As a class, the doctors have not wanted to run the rest of the world. The late President Lowell, of Harvard, said with regret that the doctor was too busy and too occupied by keeping abreast of the extraordinary medical advances to participate as he should in public affairs, and that the public was greatly the loser thereby. Nevertheless, the public has always wanted its doctors "straight," if you understand that drinking term. The public looked down its nose, and still does, at literary doctors or artistic doctors. And the doctor has shown that he is human and like other folks when he indulges in literature, art or music, usually almost secretly.

But this is not a clarion call for the doctor to dominate the world. Anyway, he knows people too well and himself too well. In his more robust and more individualistic moments, the doctor would like to be more master of his fate and his destiny. But no pedestal for him. In these days of so many words written and spoken about freedom and security, he would like a bit of that freedom in his work. And as for security, his experience makes him skeptical. He has seen diseases vanish and new diseases appear. He has seen trusted remedies become obsolete; he has seen the strong die and the weak get well; he has seen the rich become poor and the poor become rich. He knows that the world is a better and more healthful place in which to live than it was, despite wars, taxes and a large collection of pet hates and aversions of his own.

And so let us turn to a pleasant scene of two elderly doctors, fishing and talking. The fishing was not very brisk, but the talk was brisk and at times salty. Both doctors agreed that the world was in a hell of a mess and what had not already gone to hell was on its way there. Finally one doctor said to the other, "And I suppose if you had your life to live over again, and even knowing what you do, you would be just damn fool enough to be a doctor, the same kind of a doctor, and live the same life." The other doctor answered, "Yep, I suppose so, but I think I'd do more fishing."

CARDIOSPASM AS A CAUSE OF PNEUMONITIS*

WILLIAM GRAY, M.D.,† AND I. R. JANKELSON, M.D.‡

BOSTON

CARDIOSPASM results in dilatation and elongation of the esophagus and a secondary esophagitis caused by a variable degree of food retention. Whenever ingesta are retained in the esophagus, — and in cardiospasm the capacity of the esophagus may be a quart or more, — there is danger of inhalation of food, saliva or secretions, which may lead to the development of an inhalation pneumonia, lung abscess, chronic bronchitis or bronchiectasis.

Jackson and Jackson[1] have rightly emphasized that such inspiration is especially likely to occur with obstruction in the upper portion of the esophagus, particularly in the presence of a carcinoma. They describe nine means by which pulmonary symptoms can be developed by pathologic conditions in the esophagus. Of these only one applies to cardiospasm. The pulmonary involvement secondary to a pre-existing cardiospasm is due to regurgitation of food or secretions, which is particularly prone to occur during sleep when the normal protective reflexes are less sensitive. Thus food particles from the large reservoir in the esophagus may be inhaled. Sudden wakening with coughing, choking and strangling is not infrequent in cases of esophageal food retention. Moreover, Rastelli[2] and Camiel and Loewe[3] demonstrated by roentgenoscopic and roentgenographic methods frequent spilling of barium into the trachea and bronchi in obstructive lesions of the esophagus. This demonstrates that inspiration of food and secretions may occur during waking hours as well as in sleep. It is likelier to occur in debilitated, emaciated and dehydrated persons, whose reflexes, like all other body functions, are less active than those of others. Minimal inspiration leads to some strangling and coughing, and massive inhalation may lead to serious pulmonary disease.

Two such cases that recently came to our attention are reported below.

CASE REPORTS

CASE 1. C. T. (B. I. H. 71845), a 45-year-old, married woman, was admitted to the Beth Israel Hospital with a 4-year history of dysphagia and a 3-year history of vomiting and regurgitation. The vomiting occurred several times daily, the vomitus consisting of mixtures of partially digested and unchanged food. The patient frequently awoke from sleep to find her mouth full of regurgitated food, some of which had run out on the pillow. Attacks of sharp pain located in the midback region on the right side had begun 2 years previously, and as time went on this pain became more diffuse and was transmitted to the right side of the neck. Four months prior to entry into this hospital, the patient developed a cough productive of large amounts of mucopurulent material, associated with pain in the bilateral posterior part of the chest and fever. Because of these symptoms she entered another hospital. During the next 2 months she had three attacks of fever, cough and chest pain, each episode lasting about 10 days. X-ray films of the chest taken at that hospital showed bilateral bronchopneumonic changes, and although sputum and gastric washings were negative for acid-fast organisms, a diagnosis of pulmonary tuberculosis was made and the patient was transferred to a tuberculosis sanatorium for further care. During her 2-month stay there, almost continuous vomiting and regurgitation with progressive emaciation took place, and a fourth attack of high fever associated with cough, diffuse rales and patchy dullness in both lung fields occurred. This attack lasted for 9 days and did not respond to chemotherapy. Repeated sputum examinations were negative for tubercle bacilli.

FIGURE 1. *Roentgenogram of Esophagus (August 4, 1943). Fluoroscopic and roentgenographic examinations showed the esophagus to be markedly widened and tortuous. In this film the upper two thirds of the esophagus is mottled, owing to retention of food and secretions. These findings are typical of cardiospasm.*

Because of doubt concerning the accuracy of the diagnosis of pulmonary tuberculosis, the patient was transferred to this hospital for further study and treatment. At the time of entry she presented a picture of extreme emaciation, weigh-

*From the Medical Service and the Gastrointestinal Clinic of the Beth Israel Hospital.

†Assistant in medicine, Tufts College Medical School; resident physician, Beth Israel Hospital.

‡Assistant professor of medicine, Tufts College Medical School; associate physician and chief of gastrointestinal clinic, Beth Israel Hospital.

ing only 85 pounds, whereas 4 years previously she had weighed 140 pounds.

Physical examination revealed an apprehensive woman with a rectal temperature of 102° F., a pulse of 110 and a respiratory rate of 32. The pharynx was diffusely reddened and showed considerable lymphoid hyperplasia. Examination of the lungs showed dullness to percussion over both bases, with crepitant rales over the lower part of both lungs posteriorly, more marked on the right side than on the left. The heart sounds were hyperactive, and there was a harsh, blowing systolic murmur heard best just to the left of the

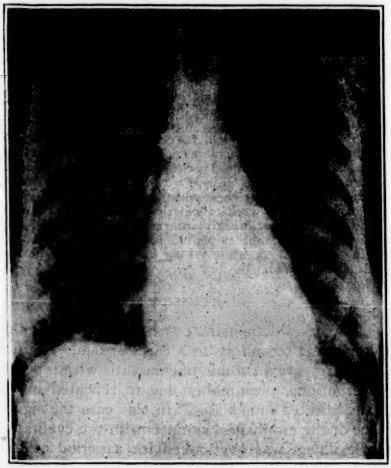

FIGURE 2. *Roentgenogram of Chest (August 4).*

This film shows mottled density involving the lower two thirds of both lungs, more marked on the right, that is consistent with bronchopneumonia.

sternum in the 3rd intercostal space, but the heart size was within normal limits. Moderately severe clubbing of the fingers and minimal clubbing of the toes were present.

X-ray examination of the chest on admission showed findings consistent with bronchopneumonic consolidation in the right upper lobe and resolving patchy pneumonic consolidation throughout both lung fields. At the time this film was taken, it was noted that the heart appeared to be slightly dilated to the right. Because of this, the patient was sent to the X-ray Department on the following day for fluoroscopy of the heart. At that time a horizontal fluid level was seen in the upper posterior mediastinum. The patient was then given a swallow of barium and it was found that the esophagus was markedly dilated and tortuous (Figs. 1 and 2). The report of this examination stated, "The convex contour previously interpreted as a dilated right heart turns out to be the contour of the tortuous, dilated esophagus typical of cardiospasm." Only small amounts of barium were seen to trickle through the cardia into the stomach. The stomach and duodenum were normal. Another x-ray film of the chest taken on the 10th hospital day showed no essential change from the previous examination. On that day the temperature rose to 104° F., with an elevation of the respirations to 50 and of the white-cell count to 20,000. Associated with this there appeared increasing signs of bronchopneumonic consolidation throughout both lungs. From the 10th to the 15th day, the temperature ranged between 101.0 and 105.5°F. X-ray examination of the chest on the 13th day showed markedly increased consolidation throughout the lower two thirds of both lung fields (Fig. 3). On the 16th day, it was finally decided that the patient had aspiration pneumonia on the basis of esophageal overflow, and she was placed on a regime of nothing by mouth, intravenous fluids, intravenous vitamins and intravenous sodium sulfadiazine. The temperature began to return to normal by the 21st day, and by the 24th day it was normal. On the 25th day, intravenous fluids and medications were discontinued and on the following day, esophageal bouginage, with Hurst bougies, was carried out. On the 27th day, the patient coughed up a tablet of phenobarbital that she had ingested 15 minutes previously. Bouginage was repeated on the 29th, 37th and 43rd days. Each time the esophageal bougies passed more easily than the time before. After each bouginage, the patient noted that less regurgitation of food occurred. The temperature remained normal until the 46th day. During that time repeated examinations of the lungs revealed only a few scattered rales.

On the 46th day, the temperature again rose to 104° F. and signs of extensive bronchopneumonia reappeared in both lung fields. Sulfadiazine was again started, but it was given by mouth, as were food, fluids and other medications. The diet consisted of fluids and semisolid foods only. The patient continued to run a spiking temperature with daily variations between 101 and 104° F. until the 59th day, when sulfadiazine was omitted. The temperature continued to be elevated until the 64th day, when it returned to normal, in association with clearing of the signs of pneumonia.

Bronchoscopy and esophagoscopy were carried out on the 56th hospital day. The only abnormal findings were a lack of active sensation and normal reaction against the procedure and cardiospasm, with atony of the esophagus. It was the opinion of the operator that the dilatation of the

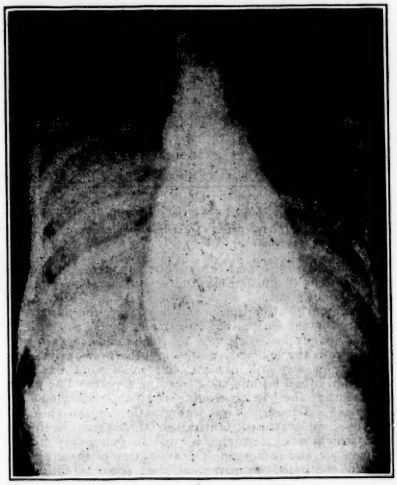

FIGURE 3. *Roentgenogram of Chest (August 17).*

This film shows increased density throughout both lung fields as compared with the previous examination. Definite consolidation is present.

esophagus, the cardiospasm and the lack of normal sensation in the esophagus and bronchial tree accounted for the spilling of food from the dilated esophagus into the respiratory tract.

X-ray examination of the chest on the 73rd day showed partial clearing of the pulmonary infiltration (Fig. 4). Fluoroscopic examination of the esophagus on the 83rd day still showed a dilated, atonic esophagus, but there was great improvement in the ease with which barium flowed from the esophagus into the stomach.

The temperature remained normal from the 64th to the 86th day, when the patient was discharged. She stated that she felt much improved and that she was able to swallow more easily than she had for years. Furthermore, regurgitation of food was almost completely absent. During the hospital stay the patient gained 10 pounds in spite of the two prolonged attacks of aspiration pneumonitis.

Four days after discharge, the patient again began to regurgitate and developed a temperature of 101.4° F., as a result of which she was readmitted. On examination only a few rales could be heard at the lung bases. The temperature returned to normal on the 2nd hospital day with the use of symptomatic therapy only. The patient was kept in the

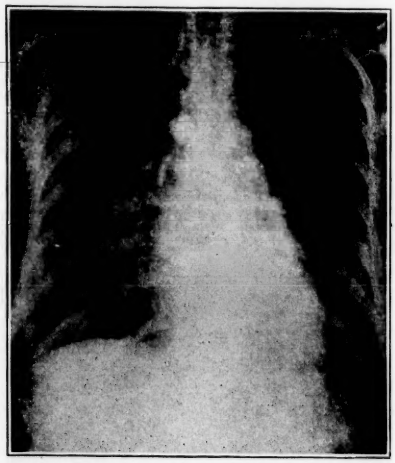

FIGURE 4. *Roentgenogram of Chest (January 19, 1944). This film shows considerable clearing in both lungs, consistent with resolving pneumonia.*

hospital for 2 weeks, and throughout this period manifested no more signs of pneumonia and no further fever; regurgitation did not recur.

Three months after the second discharge, the patient was again seen in the Outpatient Department. She was still well and her weight had increased to 108 pounds, a gain of 23 pounds from the lowest weight 4 months previously. Some regurgitation was still present, but swallowing was much easier than it had been in the preceding 4 years. The patient reported that she had no trouble at all in swallowing liquid and semi-solid foods. X-ray examination of the chest still showed some scattered infiltration throughout both lung fields, which was interpreted as due to pulmonary fibrosis. Fluoroscopic and radiographic examination of the esophagus revealed continued improvement, but some retention was still present. During these 3 months, the patient had been completely free of fever and her cough had decreased markedly. Another esophageal bouginage was done.

CASE 2. M. E., a 34-year-old woman, had had a history of dysphagia for 10 years. The amount of discomfort varied from time to time, but she was never completely free of symptoms. The difficulty in swallowing was more marked when she partook of solid food. Liquid and mushy food was swallowed with little or no distress. Throughout these years there was considerable gagging and choking. There were also frequent coughing spells and occasional bringing up of food particles. The patient had lost 18 to 20 pounds in weight and felt weak and tired. During these 10 years the patient had four attacks of pneumonia, the first episode occurring 8 years previously. Six years previously, she had a diffuse bronchopneumonia, at which time her life was despaired of, and ran a febrile course for at least 6 weeks; careful bacteriologic studies revealed no pneumococci in the sputum or the blood. Another attack of pneumonia, relatively mild in character, occurred 4 years previously. The last attack occurred 2 years previously, when the patient was again seriously ill for 5 weeks. Following the pneumonia 6 years previously, she developed a polyneuritis that was ascribed to vitamin deficiency, apparently precipitated by the prolonged fever and inability to partake of adequate food. She recovered after vigorous parenteral administration of various preparations of vitamin B. The patient presented herself for the treatment of the dysphagia, which in recent months had become aggravated and was accompanied by frequent regurgitation of undigested food.

Physical examination was essentially negative except for evidence of weight loss and moderate dehydration. Roentgenoscopic and roentgenologic examination revealed a markedly dilated and tortuous esophagus with a typical funnel-shaped subdiaphragmatic portion. No barium was seen to pass into the stomach during this examination. The following day the esophagus was dilated under fluoroscopic control and was found still to contain barium. Following this manipulation, barium was seen to enter the stomach. A complete gastrointestinal roentgen-ray examination 2 days later revealed no other disease within this tract. Roentgen-ray examination of the chest was negative.

Within the next 5 weeks, the patient had further dilatations of the esophagus at weekly intervals. The dysphagia improved markedly. She gained 12 pounds in weight and the gagging and choking while taking food, as well as between meals, disappeared.

DISCUSSION

These cases demonstrate two types of pneumonic involvement secondary to a cardiospasm. The first case represents a chronic pneumonitis with repeated exacerbations, presumably due to repeated insults to the affected lung tissue. In this case the significance of the esophageal symptoms in the evaluation of the illness was overlooked for a period of four months because of the predominance of the pulmonary symptomatology. The second case is characterized by repeated acute pneumonic processes, with long periods of intervening relatively good health. A review of recent current literature reveals only a few similar cases. Hoover[4] reported a case in which a patient with a chronic pneumonitis, apparently of five years' duration, was cured by esophageal dilatations. Tucker[5] reported a case of chronic pneumonitis in a thirteen-year-old boy who had cardiospasm. Thomas and Jewett[6] reported the case of a thirty-two-year-old man who had a greatly dilated esophagus due to cardiospasm and died of bilateral pneumonia. He had been receiving feedings of cream as part of a high-caloric diet. At autopsy, histologic examination showed the pneumonia to be of the type produced experimentally in animals by instilling oil into the lungs. Reports of lung-abscess formation, the result of inspiration of retained food in the esophagus, are more numerous, but neither this condition nor suppurative peribronchitis is discussed here.

The establishment of a causal relation may be difficult in a single case. In fact, it is undoubtedly frequently overlooked or a correct diagnosis is made only in retrospect. Jackson and Jackson[1] consider the demonstration of food residue in the pyriform sinuses an indication of esophageal stenosis in which

overflow into the larynx is a possibility. This sign should be looked for in every case of etiologically obscure pneumonitis. The demonstration of inspiration of barium into the tracheobronchial tree is convincing evidence of a causal relation. The observation that the patient coughs up food particles or, as in one of these cases, ingested tablets, should suggest the possibility of an inspiration pneumonia. Finally, a bronchoscopic examination may elicit important diagnostic evidence.

Since the right bronchus is nearer to the vertical than is the left, foreign bodies enter it more frequently than they do the left bronchus, so that most inhalation pneumonias primarily involve the right lung, but a bilateral involvement occurs in cases of massive inspiration. In such cases rapid exitus is the rule.

Repeated dilatations of the esophagus, which minimize the food retention, are recommended in the prophylaxis of inhalation pneumonia as well as in the treatment of this condition. Between attacks of pneumonia, transthoracic plastic surgery of the esophagus should be considered.

Summary

Two cases of cardiospasm complicated by inhalation pneumonitis are reported. This pneumonitis may be either of the recurrent acute type or of the chronic type with acute exacerbations. The alleviation of the cardiospasm by bouginage improves the general condition and contributes to the cure of the pneumonic process. It is recommended that the esophagus be investigated routinely in all cases of etiologically obscure chronic pneumonitis or recurrent acute pneumonia.

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Corrections. In the article "Paget's Disease: Its pathologic physiology and the importance of this in the complications arising from fracture and immobilization" by Drs. E. C. Reifenstein, Jr., and Fuller Albright, which appeared in the September 7 issue of the *Journal*, two corrections should be made. In the ninth line of the sublegend of Figure 1, the word "hyperplasia" should be "hypoplasia." In the twenty-seventh line of the first column on page 351, the figures "135/195" should be "135/95."

MEDICAL PROGRESS

PHYSIOLOGY (Concluded)*

HEBBEL E. HOFF, M.D.†

MONTREAL, CANADA

POTASSIUM POISONING IN MAN

In 1915, Smillie[47] reported a temporary episode of collapse with vomiting following the administration of 10 gm. of potassium chloride to a patient suffering from chronic nephritis with uremia. He called attention to the greatly increased toxicity of potassium salts when excretion in the urine was prevented by damage or extirpation of the kidneys in experimental animals. On the basis of these observations he suggested that spontaneous autointoxication by the potassium salts liberated in cell metabolism might occur in man if renal elimination of potassium were interrupted. This hypothesis became susceptible of proof through the work of Winkler and his co-workers,[48] who demonstrated a characteristic series of electrocardiographic changes occurring when experimental animals were poisoned with potassium administered intravenously, and who also showed that this sequence of electrocardiographic changes took place as successively higher levels of serum potassium were attained. In the absence of renal excretion of potassium, poisoning by means of orally administered potassium became possible,[49] and animals in which the kidneys were removed or the ureters tied invariably succumbed to autointoxication.[50]

Reports are now at hand indicating that an identical situation may develop in man. The first of these comes by coincidence from the Medical Clinic of the Peter Bent Brigham Hospital,[51] where Smillie's original observations were made. It concerns 2 patients with marked oliguria who were given potassium chloride by mouth as a therapeutic measure. In both patients electrocardiographic changes developed that were in every way similar to those shown by dogs in the course of potassium poisoning, and the level of serum potassium at death, examined in one of the patients, agreed with that found in the dog. The same authors[52] have now reported 2 cases in which potassium poisoning occurred spontaneously, without the administration of potassium salts. Three additional cases have been presented by Keith, Burchell and Baggenstoss[53] in which the accumulation of potassium occurred in uremia due to kidney disease.

In accord with a suggestion in an earlier progress report in this series,[54] it is now reported that in the anuria associated with the crush syndrome potassium intoxication may be responsible for death. Bywaters[55] reports as follows:

> Two thirds of the patients die toward the end of the first week, the majority on the sixth day. Death occurs very suddenly and may be preceded by cardiac irregularity. If electrocardiographic tracings are taken, changes similar to those seen in human potassium poisoning are seen — increased T waves and widened QRS complexes. These are associated with an increase of the potassium level in the serum to more than twice the normal upper level of 20 mg. per 100 cc. The raised serum potassium concentration in crushing injury is due to two processes: first, the muscle potassium diffuses out into the blood stream, its concentration falling from 300 to 70 mg. per 100 cc. or lower, both in man and in animals; secondly, very little of this is excreted owing to renal failure, and thus it accumulates in the body.

In these descriptions of fatal poisoning in man, the maintenance of blood pressure and consciousness until the onset of cardiac arrest is a striking feature, and suggests the value of electrocardiographic examination of anuric and oliguric patients. Marchand and Finch[52] mention temporary success in restoring the normal heart beat with calcium salts, and Bywaters[55] suggests the use of glucose and insulin, based on the observation (Fenn[56]) that potassium may be withdrawn from the circulation and deposited in the liver when glucose is laid down as glycogen.

The possibility of another type of potassium poisoning is suggested by the observation of an extremely high blood potassium value (287 mg. per 100 cc.) found post mortem in a woman succumbing to the effects of a soft-soap paste inserted into the uterus to produce an abortion.[57] The blood cells were completely hemolyzed, and the supposition is expressed that the potassium normally contained in the red cells was released by the hemolysis and raised the effective serum concentration to a lethal level. It is apparent, also, that although fatal potassium poisoning is not a frequent mode of death in experimental traumatic shock or adrenal insufficiency, it occasionally occurs in both of these conditions when survival is prolonged in the presence of oliguria.[58-60]

Circumstances in which the serum potassium level is abnormally low will probably prove to be more frequent and of greater clinical significance than those in which it is elevated. Familial periodic paralysis is the first well-recognized example. Occasional reports indicate that Cushing's disease may be another. Walters, Wilder and Kepler[61] reported a case that was successfully treated by subtotal resection of the adrenal glands, in which low preoperative levels (10.4 and 9.3 mg. per 100 cc.) rose to the upper limits of normal (24.6 and 25.5 mg.) after operation. McQuarrie, Johnson and Ziegler[62] noted a marked reduction in serum potassium and

*From the Department of Physiology, McGill University.
†Professor of physiology, McGill University.

chloride, associated with an increase in sodium and bicarbonate. The serum pH was 7.6, and the authors referred to the condition as "an asymptomatic alkalosis of a severe grade." This association of alkalosis and low serum potassium was observed also by Willson, Power and Kepler,[63] but in this case tetany was present. Talbot, Butler and MacLachlan[64] administered methyl testosterone and testosterone propionate to an eight-year-old girl suffering from Addison's disease in an attempt to restore muscular strength, and recorded a striking reduction in serum potassium to 1.9 milliequiv. per liter. They state:

> The marked lowering in the serum potassium concentration while the patient was receiving testosterone was not associated with clinical evidence of muscular weakness or paralysis. On the contrary, the patient seemed to benefit from the testosterone, as evidenced by gain in weight, growth in stature and apparent increase in strength and endurance.

They suggest that one of the mechanisms operating in the gain in weight was an increase in intracellular water.

From these observations, and from the experimental evidence that indicates an influence of adrenocortical and associated hormones on the level of serum potassium, Darrow[65] concludes that deficit of potassium occurs in other clinical conditions, and that unexplained high bicarbonate, low chloride and low potassium in the serum may be the findings that will lead to the discovery of cases. Two subsequent reports bear out his predictions. In a case of Addison's disease in which death occurred in heart failure, histologic changes were seen similar to those found in potassium deficiency.[66] It was thought that the heart failure resulted from a low serum potassium level, produced by a combination of desoxycorticosterone pellet therapy and a low potassium intake due largely to failure to eat. No potassium determinations were made, however, during the premortal hospitalization, and values during a previous hospital admission were normal. A bibliography of the subject of low potassium is found in this paper and in Darrow's review. Low potassium with an entirely different etiology is reported by Brown, Currens and Marchand.[67] In their 2 cases there appeared to be an excessive loss of potassium due to renal insufficiency in chronic nephritis, and the serum potassium fell to 2 milliequiv. per liter. The patients complained of extreme muscular weakness, fatigue and paralysis, the T waves in the electrocardiogram were of low voltage and the oral administration of potassium salts appeared to be of benefit.

Curare

No drug has attracted interest among physiologists equal to that curare has aroused nor proved so useful as a technical tool or as a stimulus to new investigations. Few drugs have had less clinical usefulness. Physiologists are therefore likely to watch with interest the application of this drug to a variety of purposes for which its unique physiologic properties may prove useful. The most recent and potentially the greatest use is in anesthesia, to secure or to enhance relaxation of skeletal muscle during surgical operations. It was given its first clinical trial in Montreal by Griffith,[68,69] who has employed it with considerable reservation in situations in which it is impossible or too hazardous to obtain relaxation with the anesthetic agent alone. Cullen[70] employs the drug more freely, to obtain relaxation rather than to increase the concentration of the anesthetic agent. His practice is to carry the patient in light second-plane inhalation anesthesia and, with proper doses of curare, to obtain relaxation. This is achieved by intravenous injection of at least 0.06 gm. (3 cc.) of the commercial extract (Intocostrin-Squibb), although usually 0.1 gm. is required in the average patient under cyclopropane anesthesia. Ether apparently interferes directly with neuromuscular transmission[71] and requires that the dose of curare be reduced to one third of that used during cyclopropane anesthesia. There is a report that curare has a direct depressant action on the respiratory center,[72] but the diminution in frequency and depth of respiration noted in an early stage of curarization may represent the reaction of the center to the diminution in reflex drive that must occur as skeletal muscles begin to be paralyzed and fail to set up the reflex stimulus to respiration for which they are normally responsible.[73]

Curare has also been employed to cushion the convulsions in therapeutic shock,[74] to prevent the convulsions in tetanus[75–77] and as a temporary relief in spastic states.[78] When employing the drug in these situations, as well as in anesthesia, it is necessary to remember always that the muscles of the respiratory center become paralyzed at very nearly the same level of dosage as do other skeletal muscles, and that it may therefore be necessary to employ artificial respiration. Since with the complete loss of muscle tone caused by the drug the chest has little natural elasticity, chest-pressure methods are ineffective, and those employing positive air pressures must be employed.

Detection of Time of Ovulation

Burr, Hill and Allen[79] noted that an increase occurred in the potential difference between a vaginal and a suprapubic electrode at the time of ovulation in the rabbit, and these findings have been confirmed in other species.[80–86] The same phenomenon was shown to occur in women,[87–90] and has been advocated as a means of determining the time of ovulation. The cause of the phenomenon has supposedly been electrical potentials developing between the ovary and other organs owing to rupture of the follicle. Study of such potentials in women on whom laparotomies were performed indicated that the potential changes might develop before

ovulation occurred, leading to an extensive study of the problem, which has been published recently.[91,92] The most crucial observations in this study consist in the failure to detect any potential differences between any two organs in the abdominal cavity greater than about 1 millivolt in 3 women during the course of routine laparotomies performed during the calculated ovulation time. Several follicular surfaces, including that of one fairly large, presumably mature follicle, as well as the intervening ovarian cortex, were tested, but no significant electrical potential was detected. It being concluded that the potentials measured were therefore restricted to the surface, the influence of temperature differences between recording skin surfaces was investigated, and was found to be of the average of 1 millivolt per degree Centigrade in finger-to-finger potentials. The temperature difference between vagina and various skin reference points was also found to be related to vagina-to-skin potentials. Changes in the pH of the skin were seen to affect the potentials recorded between the skin and the vagina. From these studies the conclusion was drawn that "so-called ovulation potentials previously reported, whether elicited between a vaginal and a suprapubic electrode, between two surface areas — abdominal or flank — or between fingers, are measurements only of local changes in peripheral cutaneous blood flow, owing to alterations in capillary tone." Experimental data and calculations indicate that the potential shifts may be occasioned by pH alterations induced by temperature changes.

Although these experiments render it highly unlikely that the so-called "ovulation potentials" arise directly in the ovary as the result of ovulation, they do not detract from the evidence hitherto adduced that they are indeed closely associated with ovulation in time. They do suggest that the method is possibly only a roundabout method of detecting changes in temperature associated with ovulation. Indeed, there is a recurring interest in the use of basal temperature graphs in determining the data of ovulation.[93–97] Tompkins[93] reports as follows:

> A record of body temperature taken daily under standard conditions shows a typical curve during the menstrual cycle. The temperature is relatively low during the first part of the month, drops to a minimum about the time that ovulation occurs and rises definitely thereafter to a relatively high level, which is maintained until the next menses, when the temperature drops abruptly. Before the menarche, after the menopause and in men, similar temperature fluctuations are not found. If conception occurs, the temperature will remain at the high postovulation level. The important feature is the rapid rise in temperature at ovulation.

Certain evidence in favor of this method comes from Greulich and Morris,[98] who recorded morning rectal temperatures daily during successive cycles in 14 women aged fifteen to thirty-nine years. In all of them laparotomies were performed and the ovaries were inspected. Eight women showing a characteristic postovulatory temperature rise preceding the operation were found in fact to have ovulated. Five women showed no rise in temperature before operation and were found not to have ovulated. In 1 case a slight rise in temperature began before operation, and sections from the ovary suggested that ovulation was about to take place. This of course fits in with the observation that ovulation potentials may be seen before ovulation begins.[89,90] In the belief that the temperature changes taking place during ovulation are more marked in the uterus, Klaften[97] has devised a thermometer by which uterine temperatures may be taken. The evidence he presents does not appear to indicate any decided advantages for this method.

British and American Hemoglobin Standards

For a number of years a discrepancy has been noted in the hemoglobin standards of England and of America. The English standard was that of Haldane, and was based on the color of carbon monoxide hemoglobin. According to this standard the blood of the average man contains 13.8 gm. of hemoglobin per 100 cc. and has an oxygen capacity of 18.5 cc. American workers, using other methods for determination of oxygen capacity and hemoglobin,[99] found considerably higher values, namely, 15.8 gm. of hemoglobin and 20.9 cc. of oxygen per 100 cc.[100–102] The discrepancy was at one time attributed to the greater number of automobiles in the United States, which produced a mild degree of chronic carbon monoxide poisoning, with a resultant increase in hemoglobin.[103] Little support was found for these suggestions, and it was found that, when the Van Slyke method for determining oxygen content was employed, English blood samples showed higher hemoglobin levels than were given by the Haldane hemoglobinometer[104] and that high values could be obtained in other centers of population, such as Sydney.[105] With the arrival in England of American soldiers, it became apparent that there was no difference between the hemoglobin levels in the blood of English and American soldiers, and the reputed differences must have a methodologic origin. When the Haldane standard was re-examined by a new method for assay of hemoglobin,[106] it was found that in fact it corresponded to a hemoglobin content of 14.8 gm. and an oxygen capacity of 19.8 cc. per 100 cc.[107–110] "How it has come about," state one group of workers,[110] "that this standard, which has been checked and rechecked for more than forty years, could have changed from an original equivalence of 18.5 ml. of oxygen to the present 19.8 ml. is a perplexing problem." They incline, however, to the belief that the fault lies primarily in the reliability of the Haldane method for gas analysis in blood. Whatever the cause, the English standard is now brought more closely in alignment with the American figures.

The Neurone Theory

A review by Nonidez[111] of the present status of the neurone theory reminds physiologists of the extent to which the present structure of neurophysiology is dependent on and associated with the neurone theory. His summary is quoted in full as an admirable account of the recent history of the neurone theory:

> During the last decade certain authors have considered the classical neurone theory to be obsolete and have resuscitated the long-rejected hypothesis of a nervous syncytium, mainly on histological evidence. Bauer believes in connexions between embryonic neuroblasts, serving as pathways for the growth of nerve fibers which thus develop intraprotoplasmically. This concept must be regarded as entirely hypothetical. Anastomoses found between neuroblasts and nerve fibers growing in tissue culture are emphasized by the reticularists, but this is not overwhelmingly against the neurone theory, since such anastomoses are by no means universal and they depend on the part of the nervous system cultured and on the properties of the medium. Claims by Bauer on the continuity of nerve cells with each other and with neuroglia disagree with the demonstrated existence of free dendrites and of synapses with neurones. Reticularists also maintain the continuity of neurones in the autonomic system, but this too is open to criticism on histological grounds. Moreover, autonomic ganglia afford good material for the demonstration of synaptic endings both in fixed and living preparations. The reality of independent neurones is confirmed by the degeneration of synaptic *boutons* in the central nervous system after the destruction of nerve tracts, and by the degeneration and regeneration of preganglionic fibers in autonomic ganglia, in which the loss and recovery of function are confirmed experimentally. The existence of the synapses is confirmed by the decay in impulse transmission, varying with the type of synapse, and by the nicotine block to impulses from preganglionic fibers to autonomic ganglia. The recent criticisms of the neurone theory are based on preparations made exclusively by the Bielschowsky technique, unsupported by experimental work, and the several workers disagree widely in their evidence. Boeke claims that the finer divisions of the autonomic system contain a meshwork of neurofibrils clearly distinguishable from the surrounding connective tissue; this structure is not found, however, with other neurofibrillar methods but appears with silver carbonate, which does not stain nervous structures. Stöhr believes in a fine terminal reticulum of the autonomic and sensory systems surrounding every cell in the body. Again other competent histologists, working with techniques which do not stain connective tissue, have failed to confirm Stöhr, whose claims are moreover unsupported experimentally. The reticularists cannot agree among themselves on their substitute for the neurone theory, and it would seem wise to retain this concept until better proof is offered of the syncytial nature of the nervous system.

Origin of Heart Beat

The cause of the heart beat presents perhaps the oldest and most controversial problem in physiology; a great part of it is now of historical interest only.[112, 113] So far as the vertebrate heart is concerned, the long disputes between adherents of the neurogenic and myogenic theories may be said to have resulted in the complete victory of the latter doctrine. However this may be, recent evidence indicates that in acting as pacemaker to the heart the muscular tissue of the sinus venosus or sino-auricular node behaves very much as does a nerve fiber, nerve cell, sense organ or even skeletal muscle in certain circumstances.

With the discovery of the refractory period in the heart,[114] it became possible to construct the first rational theory of the origin of the heart beat, as due to the presence of a constant inner stimulus, which set up a beat whenever the heart recovered sufficiently from the refractoriness caused by the previous discharge. This simple explanation appears to account for the repetitive firing of a nerve fiber injured at one end, the local injury current acting as the constant stimulus. In the nerve cell this explanation proved inadequate to account for the relatively slow rhythms exhibited by such neurones as the soleus motoneurone, in which the interval between beats is many times the known absolutely refractory period. With the recognition of the subnormal period, this problem was solved, for it was realized that the motoneurone may show a depression of irritability long outlasting the absolutely refractory period, and that discharge can only occur at the end of this period, when the threshold falls toward normal.[115] In the heart even this extension of theory proves inadequate, because it has been repeatedly found that a gradually falling threshold is only occasionally seen, and that usually the threshold remains level for some time before a new beat occurs. This is particularly true of the pacemaker itself, where, in fact, a period of supernormal recovery is at times found.[116] This obviously indicates that the inner stimulus of the heart cannot be constant in intensity but is intermittent. This is now established in the vertebrate heart through the work of Bozler,[117–119] who has studied electric potentials in pacemakers in the smooth muscle of the ureter and small intestine, and in turtle, dog, cat and guinea-pig heart muscle. Apparently pacemaker activity is the result of the spontaneous development of slow rhythmic oscillations of potential, which are found only in pacemaking tissue. These potentials are closely allied to rhythmic oscillations between the negative and positive after-potentials, and if they are sufficiently intense, — about one fiftieth of the normal spike potential, — propagated discharges are set up at their negative crests. These spontaneous, slow, potential changes — so-called "prepotentials" — are apparently the direct cause of the heart beat. They may be increased, or even developed in the heart, by anodal polarization,[120] and in nerve and skeletal muscle their appearance is facilitated by low calcium and alkalinity.[121–123] Although the point has not been settled, it is possible that the so-called "pre-sinus" waves noted by Rijlant[124] represent prepotentials in the mammalian pacemaker.

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DIFFERENTIAL DIAGNOSIS

DR. FLETCHER H. COLBY: In the first admission there is a long history of pain in the lower abdomen and of backache, with a hospital admission in which the essential findings were fever, leukocytosis, lower abdominal tenderness and evidence of peritoneal irritation. At that time a mass was felt in the left side of the pelvis and there was evidence of inflammation of the glands of Skene and Bartholin. With bed rest, intravenous fluids and chemotherapy this acute illness subsided. A reasonable explanation for this episode seems to be an acute flare-up of a pelvic inflammation.

In about two months the patient returned to the hospital with pain and tenderness in the lower abdomen, and what I should suppose was a recurrence of the low-grade pelvic inflammatory process. At that time there was no fever or leukocytosis, and there was but little abdominal tenderness. There were, however, costovertebral tenderness on the left and hematuria. I assume that the hematuria was total, and that the urine was grossly red.

DR. RONALD C. SNIFFEN: Yes.

DR. COLBY: Considerable blood was present in a catheterized specimen of urine. The previous urine was acid, with a low specific gravity and a few pus cells. Evidence that was obtained by cystoscopic, x-ray and pyelographic examinations strongly suggests that the left kidney was the source of the bleeding. At least no note was made of a tumor in the bladder or of any acute inflammatory process of such magnitude as to result in obvious bleeding. Gross bleeding in the urinary tract in the majority of cases — at least 70 per cent — is due to stone, tumor or tuberculosis; in approximately 25 per cent it is due to nontuberculous inflammatory lesions, and in the other odd 5 per cent it is caused by various blood dyscrasias and so forth. So I think that we can fairly assume that this woman had a process in the left kidney that was one of the first three possibilities.

Is there any way of connecting the previous entry with the second entry and the left renal lesion? She might have had a tuberculous pelvic inflammatory process all the time, and it is possible that the left kidney was the site of a primary tuberculous lesion that gave a filling defect. Such lesions are the rare tuberculomas that are found sometimes in the kidney and occasionally in the bladder. It hardly seems likely that this woman had tuberculosis because of the lack of persistent severe bladder symptoms and the lack of any described bladder or vesical changes on cystoscopic examination. So it seems reasonably certain that the pelvic inflammatory disease and the renal disease were two separate things. The diagnosis of the lesion in the left kidney depends entirely on the interpretation of the pyelogram.

DR. MILFORD SCHULZ: This is the film made thirty minutes after the intravenous injection of the dye. You can see the large right kidney and the large left kidney, which has only a little dye in the calyxes. This is the shadow thought to be a stone, but on the retrograde pyelogram it is shown to be outside the ureter. The upper calyxes are not greatly dilated, but there is a mass projecting from the lateral margin of the left kidney that can almost be traced around the defect in the pelvis and that deforms the middle and lower calyxes.

DR. COLBY: Will you look at this flat film and tell me if there is any irregularity of the renal outline.

DR. SCHULZ: Yes; on the left side. You can see it here on the retrograde film. I do not see any evidence of metastases in the bones.

DR. COLBY: The filling defect in the lower end of this kidney seems to be the important sign.

What are the possibilities? In the first place, it might have been a nonopaque stone; in the second place, a tumor of some sort — neoplasm or a blood clot. Nonopaque stone is a difficult diagnosis to make. Air pyelograms are helpful in the majority of cases, as in those of uric acid stone, but at times one cannot diagnose a stone by any means we have of visualization of the interior of the kidney. There is no evidence of calcification in the plain film in this region, and the patient's history somehow does not suggest the presence of nonopaque calculus. Renal pain had not been severe or significant in the history. It was an acute episode accompanied by profuse gross hematuria.

This story suggests a malignant tumor of the left kidney. There are two varieties of tumors — those that arise from the parenchyma and those that arise from the renal pelvis. If we say that it was a neoplasm involving the left kidney, which one was it? My experience with tumors primary in the renal pelvis has been that they involve the pelvis, and the pelvis in this case does not seem to have been involved. I have never seen a primary tumor of the pelvis of the kidney involve a localized area, such as one calyx, but I suppose that it is possible. Against that is the lack of function of this kidney. Function as a general thing was poor from the left kidney, which suggests, not a localized tumor of the renal pelvis, but a tumor involving the parenchyma. Such tumors, as a rule, are renal-cell carcinomas.

DR. OLIVER B. COPE: You exclude an infection, such as tuberculosis?

DR. COLBY: There is no report of a culture.

DR. COPE: What about the x-ray findings?

DR. COLBY: I have to take the evidence that is given.

DR. FULLER ALBRIGHT: Could it have been a polycystic kidney?

DR. COLBY: It was unilateral; I have never seen a case of unilateral polycystic disease, although they have been reported. In the x-ray films there is nothing to suggest to me that a bite had been taken out by a cyst. The defect is irregular, suggesting a tumor or blood clot.

CLINICAL DIAGNOSIS

Renal tumor.

DR. COLBY'S DIAGNOSIS

Renal-cell carcinoma.

ANATOMICAL DIAGNOSIS

Polycystic kidney.

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: The specimen proved to be a polycystic kidney. It was of normal contour, as most of them are, and about twice the normal size. Externally and internally it was riddled with cysts, so that there was little parenchyma — just two or three islands of recognizable cortical tissue. The pelvis and calyxes were dilated, but not greatly distorted. I do not believe that this kidney explains all the patient's symptoms; in all probability the first symptoms were due to pelvic inflammatory disease.

DR. ALBRIGHT: What was the x-ray diagnosis?

DR. SNIFFEN: Neoplasm of the left kidney.

DR. COLBY: And the preoperative diagnosis?

DR. GEORGE G. SMITH: I operated on this patient, and the preoperative diagnosis was renal tumor.

DR. COLBY: That makes me feel better.

DR. SNIFFEN: The cause of death in patients with polycystic kidneys is assumed to be a gradual enlargement of the cysts without increase in number, with consequent atrophy of the remaining parenchyma. In a few cases, however, there is the added factor of hypertension, following vascular changes in the kidney. In such cases, renal failure can be explained, at least in part, by a severe nephrosclerosis.*

DR. LLOYD MILLS: In the absence of more information about the urine, what do you think was the cause of the pain?

DR. SNIFFEN: Several things may cause pain, among them hemorrhage into a cyst and clotting of blood in the ureter.

DR. SMITH: A cyst will rupture into the pelvis. I have seen it happen with a solitary cyst, producing hematuria and a filling defect, a picture similar to that in this case.

In my operative note I said that the reason for removing the kidney was that the function was poor. It was obviously polycystic disease at operation. The other kidney was apparently carrying on the work. The blood nonprotein nitrogen was normal, and I thought that the patient would get into further trouble if the kidney were left in.

DR. SNIFFEN: The chances are that there was at least some degree of polycystic disease on the other side.

DR. SMITH: That may be true. On the other hand, a patient from whom I removed a polycystic kidney twenty years ago is still in excellent health.

Years ago we used to have a great deal of argument in the American Urological Association about polycystic disease. One member maintained that polycystic disease was unilateral as frequently as bilateral. A number of cases were discussed.

DR. SNIFFEN: Unilateral polycystic kidney does occur, but such cases are far in the minority.

DR. SMITH: Not over 5 per cent, I should say.

*Ritter, S., and Baehr, G. Arterial supply of congenital polycystic kidney. *J. Urol.* **21**:583-592, 1929.

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TREATMENT OF MENINGOCOCCAL MENINGITIS

In few conditions have the sulfonamide drugs proved of greater value than in certain types of bacterial meningitis, particularly meningococcal meningitis. The case fatality rate of epidemic meningitis was about 40 per cent in Army camps during World War I, in spite of the fact that intensive treatment with antimeningococcus serum was used. During the present war the over-all mortality from this disease in the Army and Navy is well under 5 per cent, and in several large posts 100 or more consecutive cases have been treated with fatality rates of 2 per cent or less. Furthermore, there has been a remarkably low incidence of complications.

These brilliant results have been obtained with a relatively simple treatment — the oral administration of sulfonamide drugs, supplemented when necessary in severe cases by the intravenous injection of their sodium salts.[1] This is in contrast to the traumatic and cumbersome methods formerly used — the intravenous and intrathecal injection of serum. Antimeningococcus serums are still used by some medical officers and civilian physicians, perhaps because they prefer to cling to tradition or because they assume that serum therapy is an essential part of "doing everything possible." There seems to be little, if any, reason for believing that this supplementary form of therapy is of additional benefit. Indeed, there is increasing evidence that antimeningococcus serum, particularly when given by the intrathecal route, may actually do more harm than good in most drug-treated cases.

The sulfonamides have also been highly effective in the management of meningococcus carriers, particularly the mass elimination of such carriers from large military units. The latter can be accomplished by a single dose or by one short course of a few grams of a sulfonamide drug given orally in a single day and is, likewise, in sharp contrast to the cumbersome, and usually unsuccessful, methods employed during World War I.

Drug-fastness is a serious problem in the sulfonamide treatment of infections with the gonococcus, an organism that is closely related biologically to the meningococcus, and increasing numbers of sulfonamide-resistant cases of gonorrhea are constantly being encountered in all parts of the world where these drugs are widely used. Among the sulfonamide-treated cases of meningococcal meningitis there have been some failures, particularly in fulminating acute cases and in late and neglected ones. There have also been some apparent failures, owing to the improper control of therapy, which resulted in renal or other complications and which vitiated or obscured the beneficial effects of the drug. There have been few, if any, authentic cases, however, in which the sulfonamide resistance

of meningococci obtained from human cases was bacteriologically proved.

With the introduction of penicillin and the demonstration of its effectiveness in the treatment of various infections, it was natural to explore its potentialities in all fields. The good results obtained with sulfonamides and the limited supply of penicillin did not permit early and extensive trials of the latter agent in meningococcal infections. Hence, only a small number of cases were included in the first extensive reports covering the clinical use of penicillin. In spite of the small number, it was evident that the results obtained with penicillin in meningococcal meningitis were not dramatic and that failures were encountered, particularly in cases in which sulfonamides had not been used.

Elsewhere in this issue of the *Journal* there is a report of an intensive study of a small group of cases of meningococcal meningitis treated with penicillin alone. The bacteriologic as well as the clinical results in these cases were quite disappointing when compared with those usually obtained with sulfonamides. So far as it is now known, cases of meningitis require intrathecal as well as parenteral treatment with penicillin to control the meningeal infection. This is accompanied by a definite and not insignificant inflammatory reaction, manifested by an increase in the pleocytosis of the spinal fluid and often by exaggeration of the signs and symptoms of meningeal irritation. These reactions are undesirable and often harmful, since they may interfere with the prompt bacteriologic cure and may prolong and aggravate the clinical symptoms. The parenteral and intrathecal use of penicillin, and even its use as a spray, have apparently failed also to rid the nasopharynx of meningococci.

The results in this series of cases were obtained with doses of penicillin that are usually considered to be adequate and in cases in which care had been taken to eliminate any effect of sulfonamides. The authors found out that the latter — that is, the exclusion of sulfonamide therapy — is essential in evaluating the effect of penicillin in cases of meningococcal infection.

Some good results following the use of penicillin in experimental and clinical meningococcal infections have been recently reported. Experimental infections, however, are not comparable to clinical cases of meningitis; moreover, the results were not nearly so good as those obtained in experimental infections with other organisms, such as pneumococci and streptococci. In the clinical cases, as previously stated, the actual role of the penicillin cannot be evaluated unless the effects of sulfonamides are excluded. Unfortunately, this point is not stressed in these reports — for example, that of Rosenberg and Arling.[2] There, it is stated that the only fatal case in the series did receive a sulfonamide drug. Furthermore, the fact that negative primary cultures and smears of the spinal fluid were obtained in 15 of the 65 cases strongly suggests that a sulfonamide had been given in these 15 cases and perhaps in many of the other cases before the initial dose of penicillin.

For practical purposes it may be said that sulfonamide drugs still constitute the treatment of choice in meningococcal meningitis. Penicillin therapy is more laborious, more traumatic and more expensive, in addition to being less effective in curing the meningeal infection and in eliminating the carrier state. From the information thus far available it seems wise to reserve penicillin for use as an adjunct to the sulfonamide drugs in those cases in which the latter do not bring about an adequate clinical response or for use in cases in which sulfonamide drugs cannot be given. Penicillin may also prove helpful in the management of focal purulent meningococcal infections, particularly those of the joints. Withdrawal of synovial fluid and intra-articular injection of penicillin may hasten the bacteriologic cure of such infections. It is not clear from present reports whether the clinical results of the use of penicillin in such focal complications are superior to those observed with sulfonamides.

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MINIMUM CURRICULUM AND SYLLABUS FOR SCHOOLS OF NURSING

THE Massachusetts Authority for Schools of Nursing has just issued a booklet to guide nursing schools in the construction of their curriculums. In the preface it is explained that this represents the joint effort of representative physicians and nurses to agree on what should be included in the ideal course of nursing. The impossibility of devising an inflexible statement of what should be included and what should be deleted is recognized, and is met by placing an asterisk opposite the subjects that are deemed most important. This, of course, represents a compromise between the thinking of those who wish to elevate the profession of nursing onto higher and more scientific levels and those who wish to extend its practical applications over a wider field of availability and usefulness — two aims that are quite diverse.

The same controversy exists in medical education: there are those who would exalt science and research exclusively and those who think that doctors should be trained merely to care for the sick population. Neither of these attitudes should be permitted to develop to any extreme degree or to the exclusion of the other. It is true that the outstanding individuals in any profession rise by their own innate aptitudes fully as much, or more, than by the schooling to which they are exposed. Without the schooling, on the other hand, they lack the sanction of authority — they are "irregulars," if such a noun is permitted, and there are irregulars in both camps.

The syllabus represents a nice balance between these educational elements. It will undoubtedly be a most useful and much-needed guide to those who are interested in the training of nurses, but it will naturally need periodic revisions and occasionally rewritings. The *Journal* welcomes it as an unusually competent statement concerning an important educational problem.

MISCELLANY

NOTE

The Board of Overseers of Harvard College at their regular meeting on September 25 approved a recommendation of the Faculty of the Harvard Medical School that women students be hereafter eligible for admission to the school. The recommendation had been previously approved by the Harvard Corporation and will become effective for students entering the school in the fall of 1945.

CORRESPONDENCE

BASAL TUBERCULOSIS

To the Editor: It was with great pleasure that I read the article by Dr. Emil Z. Ossen in the June 8 issue of the *Journal*. He treated the subject of basal tuberculosis in a masterful manner because the disease, being as uncommon as it is, often presents an annoying diagnostic problem. I might mention that we have seen a few cases over here that exemplified the material presented by Dr. Ossen.

At present, we have a young soldier of twenty-three who has basal tuberculosis in the upper portion of the left lower lobe. He, of course, will be sent back to the United States shortly. A history of familial contact, the physical findings, x-ray slides and the laboratory evidence are conclusive. When seen on sick call a few days ago, he presented only a few signs of pathology, namely, a low-grade fever (99.5°F.) and a few localized subcrepitant rales below and medial to the lower angle of the scapula. He felt quite well systemically — no lassitude, apathy or weakness. He was somewhat apologetic for coming on sick call. He had no history of anorexia, loss of weight, hemoptysis, night sweats or other evidence of tuberculosis. His history was one of parental exposure fifteen years previously, and none since then. Atypical pneumonia was believed to be the diagnosis when he was admitted to the hospital. Sputum taken immediately to the laboratory proved positive for tubercle bacilli. X-ray films showed a basal lesion, and none in the apex. A cavity was seen in the involved area. I should call this a "pure type." It is a fulminating type, I believe, in view of the lack of prodromal symptoms and the positive sputum. Frankly, I consider this type of tuberculosis somewhat terrifying because I believe that its detection can, at times, be extremely difficult. As mentioned in Dr. Ossen's article, bronchiectasis, neoplastic disease, pulmonary abscess and even mycoses can be ruled out rather easily most of the time. I am not quite so certain about atypical pneumonia, especially if negative sputums are obtained, as they are often at the onset of the disease. Pneumonitis certainly can appear on x-ray examination at a situation similar to that of the earliest stage of basal tuberculosis.

So far as the diagnosis of atypical pneumonia goes, over here we see far more unilateral than bilateral involvement, at least in the severe forms, which are not infrequent. Most of the medical officers here believe that this disease is transmitted from person to person by the usual droplet method, a theory that is not generally accepted by the profession. Furthermore, most of these patients show few physical signs for two or three days, and these usually are a few localized rales and nothing else. X-ray films show a picture similar to that of pneumonitis. Most of the patients stay in the hospital with a low-grade fever for two or three weeks. Treatment, of course, is symptomatic. Atypical pneumonia as seen over here certainly must be ruled out in these cases.

A final word about tuberculosis. I believe that a young person with long-continued fever and minimal pulmonary involvement has a graver prognosis than an older person with extensive involvement but with little fever. This is not exactly my own idea, but it has been impressed upon me during my tenure in the Army.

In conclusion, the matter brings out the old axioms and rules for practicing good medicine — CAREFUL HISTORY, CAREFUL PHYSICAL EXAMINATION, AND CAREFUL AND COMPLETE LABORATORY EXAMINATION.

I. ROBERT FRANK
Major, Medical Corps, A.U.S.
Southwest Pacific Area

BOOK REVIEWS

The Inner Ear, Including Otoneurology, Otosurgery, and Problems in Modern Warfare. By Joseph Fischer, M.D., and Louis E. Wolfson, M.D. 8°, cloth, 421 pp., with 77 illustrations and 7 tables. New York: Grune & Stratton, 1943. $5.75.

This book, considering the senior author's excellent record as a teacher and contributor in this particular subject, fails to accomplish what the aim expressed in the preface — a simplified discussion of the inner ear. The fault does not lie with the contents of the book but mostly in the manner in

which it was printed and illustrated. The illustrations, particularly the photographs of temporal bone and skull, are not well reproduced. The reader therefore misses much of the subject matter because of the lack of comprehensive illustrations. The experienced otologist will enjoy reading the chapters dealing with physiology and anatomy, which are interestingly presented.

There is a definite need for a treatise of this kind for otologists, neuro-otologists and neurosurgeons. In the next edition the authors in all probability will overcome these not too serious defects.

A Clinical and Experimental Investigation of the Blood Cholesterol Content in Myxoedema and Other Conditions. By E. H. Stokes, M.B., Ch.M. (Sydney), F.R.A.C.P. 4°, cloth, 121 pp., with 13 illustrations. Sydney: Australasian Medical Publishing Company, Limited, 1941.

The writer of this monograph happened to become interested in cholesterol metabolism through seeing a patient with myxedema and hypercholesterolemia. This was nineteen years ago. Ever since then the riddles of cholesterol metabolism have fascinated him, and in 1928 he began to attempt to solve them by systematic study.

The result of all the work that he has done in this field is now printed. The author writes easily, so that what he says is well expressed. He is a good student of literature, so that he has compiled a useful bibliography. He is conservative in his conclusions, so that he modestly admits there still are many undiscovered factors other than a deficiency of thyroid that may play a part in producing hypercholesterolemia in myxedema.

On the whole this book will prove a useful one for reference. It is especially pleasant to welcome it as a fair sample of the type of medical investigation now going forward in the laboratories and wards of our Australian colleagues.

Strabismus: Its etiology and treatment. By Oscar Wilkinson, M.D., D.Sc. In collaboration with Richard W. Wilkinson, M.D., M.Sc. (med.). Second edition, revised. 8°, cloth, 369 pp., with 71 illustrations. Boston: Meador Publishing Company, 1943. $4.00.

The second edition of this book, with the chapters on nonsurgical and surgical therapy largely rewritten, and with ample recognition and citation of authorities throughout the text, offers an ideal review of the problems in strabismus for the young ophthalmologist.

Adequate attention is given to etiology and types of strabismus, to methods of examination of the patient, and to nonoperative and operative therapeutic procedures and their indications. The text is concisely and interestingly written and is amplified by numerous illustrations and drawings. Forty pages are devoted to illustrative cases, with essential items from the case history, and photographs before and after treatment.

Life Is Too Short: An autobiography. By C. Kay-Scott (Frederick Creighton Wellman. M.D.). 8°, cloth, 348 pp. Philadelphia: J. B. Lippincott Company, 1943. $3.50.

Dr. Frederick Creighton Wellman, also known under the name of C. Kay-Scott, is one of the few people who appears in *Who's Who in America* under both names. He has led a most extraordinary life and his volume of reminiscences is an interesting autobiography of a man of many careers.

His grandfather, a physician born in Virginia, served in the Civil War on the Confederate side. He later moved to Missouri, where the author was born in Independence. His father became a missionary to Indian tribes, and the son always had a desire to become a missionary physician. After graduating from the Kansas City Medical College and serving as an intern in the Kansas City Public Hospital, he went to Central Africa, where he lived for a number of years as the medical officer to an American mission. There he did considerable research in pure science, as well as in medicine, particularly in zoology and entomology. He published an elaborate monograph on the fevers found in Central Africa, as well as several articles on plants and a systematic, annotated check list of insects. He thus was brought quickly into the scientific world and became well known in England and elsewhere as a student of entomology. Later, he went to California, where he taught at San Francisco, and ultimately to New Orleans.

Following that period of his life, he journeyed to Brazil, gave up the practice of medicine and became a mining engineer. He then turned to the field of literature, wrote novels and began to paint, changing his name to C. Kay-Scott. Thus he began a new career, in which he was eminently successful, for in addition to his painting, which was widely admired, he eventually became director of the Denver Art Museum and dean of the College of Fine Arts at the University of Denver. Ultimately, he was reunited with his family, from which he had been long separated. During his life he was married and divorced a number of times, but it was with the children of his first wife that he finally found himself happily reunited, looking back on an extraordinary career.

This autobiography is somewhat overwritten, but a physician will find much of interest in the book regarding an unusually talented man — physician, missionary, scientist, explorer, mining engineer, novelist and painter.

Internal Medicine in General Practice. By Robert P. McCombs, M.D. 8°, cloth, 694 pp., with 114 illustrations. Philadelphia: W. B. Saunders Company, 1943. $7.00.

The author has written a classic type of practical textbook in an abbreviated form. He frankly states that he has had to appear dogmatic to achieve brevity, which lessens classroom value, but the book is well and entertainingly written, with more than a modicum of common sense through its pages.

The section on diagnosis follows orthodox lines. It is to be noted that the Hinton test is not included in the serologic tests for syphilis. The chapters on the heart, urinary tract and gastrointestinal tract are unusually complete for so small an edition, the last including a section on gastroscopy. The chapter on nutritional deficiencies is free from fantasy.

The blood dyscrasias are well covered. Infectious diseases are brought up to date, and there is an excellent chapter on the sulfonamide drugs, with an unusual listing of diseases in which the sulfonamides are not indicated. There is a brief note on penicillin. Chronic lung diseases and rheumatic disorders are ably discussed, and there is a chapter on the endocrine disorders. The field of allergy is briefly considered, and neurology and psychiatry are covered by a brief chapter on common neurologic and psychiatric problems.

The book is illustrated with excellent photographs, well-devised diagrams and a number of carefully selected x-ray plates.

The Nature and Treatment of Mental Disorders. By Dom Thomas Verner Moore, O.S.B., Ph.D., M.D. With a foreword by Edward A. Strecker, M.D. 8°, cloth, 312 pp. New York: Grune and Stratton, 1943. $4.00.

Throughout this book the author maintains a benignly middle-of-the-road course that enables him, without crowding, jostling, or conflict, to salute Kraeplin, Freud, Jung, Adler, psychosomatics, neurology, statistics, commonsense and a number of other things and people of importance in psychiatry. Such benignity is especially becoming to the author as a member of the Order of Saint Benedict.

In his broad empiricism he includes his own psychiatric speculations and conclusions and a summary of investigative work that he himself has conducted and published earlier and elsewhere. Since the book is brief, his presentation of so many topics is certainly in some, and perhaps in most or all, of the cases necessarily superficial.

On the credit side his eclecticism enables him to display a wide range of psychiatric resources and methods — and, incidentally, he shows himself deft and resourceful in their utilization.

Throughout the book, general discussion is amplified by a large number of case histories. These are presented vividly and, as a rule, briefly; and in every case his analysis of therapeutic procedure is clear, and his estimate of therapeutic accomplishments is a model of honesty.

Elements of Medical Mycology. By Jacob H. Swartz, M.D. With an introduction by Fred D. Weidman, M.D. 8°, cloth, 179 pp., with 78 illustrations. New York: Grune and Stratton, 1943. $4.50.

This excellent elementary text, covering the organisms commonly encountered in the United States, fills a distinct need in medical mycology. In the general discussion, the principal morphologic characters are defined and accompanied by line drawings; the commoner genera are listed with the organs usually attacked and the names of the diseases produced. This is followed by a detailed account of the laboratory methods for the confirmation of the clinical diagnosis that the author has found most useful in his practice.

The chapter on the yeast-like fungi is largely clinical and therapeutic, with little detail on the organisms involved beyond the information necessary to refer them to this group. The trichophytons producing various tineas are treated in much more detail. Blastomycosis (Gilchrist's disease), coccidioidal granuloma, chromomycosis, sporotrichosis, actinomycosis, tinea versicolor and histoplasmosis are grouped in a chapter of miscellaneous organisms, followed by a short chapter on common contaminants. A brief chapter on immune reactions and one on the effects of sulfanilamide and its derivatives, an extensive glossary and a folding chart presenting the salient features of the book in tabular form complete the work.

Although this book may seem oversimplified to the specialist in this field, it should prove a valuable text for the beginner and for the busy clinician. It is unfortunate that the author has placed the organism of Gilchrist's disease among the Blastomyces in violation of the international rules of botanical nomenclature and has confused the clinical pictures of Brazilian blastomycoses caused by *Paracoccidiodes brasiliensis* and by *P. cerebriformis*. The illustrations of lesions are well chosen, and the photomicrographs of the organisms are excellent.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Handbook for the Medical Secretary. By Miriam Bredow, dean of women, Eastern School for Physicians' Aides. 8°, cloth, 253 pp., with 18 illustrations. New York: McGraw-Hill Book Company, Incorporated. 1934. $2.25.

This manual is written for medical secretaries who are already employed and also as a text for students training for the various phases of work to be found in the office of a physician. A valuable vocabulary of approximately 2000 medical terms is appended to the text. Pronunciation is given for the words uncommon to the layman. The vocabulary is divided into subjects, and would be more useful if it had been arranged in one alphabet.

The Permeability of Natural Membranes. By Hugh Davson, D.Sc., associate professor of physiology, Dalhousie University, Halifax, Canada, and James Frederic Danielli, D.Sc., A.I.C., Beit Memorial Research Fellow and Fellow of St. John's College, Cambridge, England. With a foreword by E. Newton Harvey, Ph.D., professor of physiology, Princeton University, 8°, cloth, 361 pp., with 73 illustrations and 72 tables. New York: The Macmillan Company, (Cambridge, England: University Press), 1943. $4.75.

The authors have brought together in this volume the existing knowledge of cell permeability.

Traumatic Injuries of Facial Bones: An atlas of treatment. By John B. Erich, D.D.S., M.D., consultant in laryngology, oral and plastic surgery at the Mayo Clinic, and assistant professor of plastic surgery, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota; and Louie T. Austin, D.D.S., head of Section on Dental Surgery at the Mayo Clinic, and associate professor of dental surgery, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota. In collaboration with Bureau of Medicine and Surgery, United States Navy. 12°, cloth, 600 pp., with 333 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. $6.00.

The present war has shown a decided increase in serious facial injuries, the treatment of which is becoming more and more complex. The large experience of the authors at the Mayo Clinic has been drawn on in presenting treatment for the various types of injuries of the facial bones. The major portion of the work is given up to a discussion of fractures of the facial bones. A small portion is devoted to bone and skin grafting, wiring and splinting.

An Atlas of Anatomy. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.), professor of anatomy, University of Toronto. Volume II. *Vertebrae and vertebral column, thorax, head and neck*. 4°, cloth, 184 pp., with 232 illustrations. Baltimore: The Williams and Wilkins Company, 1943. $5.00.

This is the concluding volume of an atlas designed to meet the needs of teachers and students, physicians and surgeons. The regional presentation, which is based on American methods of dissection, makes the atlas of permanent value in clinical work. The illustrations were taken from actual specimens, and the accuracy of the plates was checked by photographic means. The observations and comments that accompany the illustrations are not exhaustive descriptions but are designed to attract attention to salient points that might otherwise escape notice. The color work is good, reminding one of the best German atlases.

Education and Health of the Partially Seeing Child. By Winifred Hathaway. A publication of the National Society for the Prevention of Blindness, Incorporated. 8°, cloth, 216 pp., with 34 illustrations and frontispiece. New York: Columbia University Press, 1943. $2.50.

This valuable monograph on a sociologic subject is of great importance to the community, since it has to do with the child who is usually a misfit in the public schools. Mrs. Hathaway is an authority on blindness and in this book explains the principles underlying educational procedures and health service for partially seeing children and shows that they may be applied to further the education and health of these children wherever they may live. She describes specifically the equipment, mechanical devices and teaching methods that are available and also discusses the various problems of classification, supervision and financing that are involved in an education program for partially seeing children. The book is designed for all persons, including parents, who are responsible for the partially seeing child. It is interesting to note that the first class in the United States established especially for partially seeing pupils was inaugurated by the Boston School Committee in 1913. This text should serve as an authoritative reference source on its subject.

On the Influence of Trades, Professions and Occupations in the United States in the Production of Disease. By Benjamin W. McCready, M.D. With an introductory essay by Genevieve Miller, M.A. 12°, cloth, 129 pp. Baltimore: The Johns Hopkins Press, 1943. $1.75.

The text of McCready's prize dissertation, originally published in New York City in 1837, is reproduced in full. In the introduction, Miss Genevieve Miller, assistant at the Institute of the History of Medicine, Johns Hopkins University, comments on the conditions of industry in the United States at the time of McCready's dissertation. She also discusses briefly the life and work of McCready and proceeds to analyze his monograph. In preparing his essay on occupational diseases in America, McCready endeavored to obtain information on the subject by writing letters and interviewing workmen but without much success. He also tried to consult the books of various trade organizations to find material on mortality rates, but again was disappointed since there were no records at all or only imperfect ones. Therefore, with such scanty material he depended rather extensively on a book by Thackeray on occupations, published in London in 1851. He included also personal observations made when he was house physician at the New York Hospital. Miss Miller characterizes the McCready essay as the first American treatise on occupational diseases. Thirty-one types of employment, divided into four sections, are discussed, and in her introduction she points out those details that are additions to the previous literature. She concludes that the essay was a remarkably mature and realistic ap-

proach to the problem of occupational diseases as they occurred in the early nineteenth century in America. The essay was published in the *Transactions* of the Medical Society of the State of New York, and since only one hundred copies were printed, did not attract much attention and was not widely read. This reproduction of the text, with the scholarly introduction, is a valuable contribution to the history of the subject, and also to the history of medicine in the United States.

Functional Disorders of the Foot: Their diagnosis and treatment. By Frank D. Dickson, M.D., associate professor of clinical surgery, Medical School, University of Kansas, and orthopedic surgeon, St. Luke's, Kansas City General and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas; and Rex L. Diveley, M.D., colonel, M. C., A. U. S., and orthopedic surgeon, St. Luke's, Kansas City General, Research and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas. Second edition. 8°, cloth, 352 pp., with 202 illustrations. Philadelphia: J. B. Lippincott Company, 1944. $5.00.

The second edition of this book, first published in 1939, has been completely revised and rewritten, and much new material has been added to the text. Two new chapters of timely interest have been inserted: one on functional disorders of the foot in relation to military service, and the other on foot disorders in relation to industry. The chapter on constitutional disease affecting the feet has been entirely rewritten.

The American Illustrated Medical Dictionary. By W. A. Newman Dorland, M.D., Lieutenant-Colonel, M.R.C., U.S.A., and member of the Committee on Nomenclature and Classification of Diseases, American Medical Association. With the collaboration of E.C.L. Miller, M.D., Medical College of Virginia. Twentieth edition. 8°, cloth, 1668 pp., with 885 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. $7.50.

This new edition of an authoritative reference work has been completely revised with additions and alterations on every page. Many hundreds of new words have been included, particularly in the fields of biochemistry, chemotherapy, allergy, endocrinology, vitamin research, tropical and parasitic diseases and mycology. Special attention has been devoted to the vocabulary of war medicine and surgery, as well as to the great number of new synthetic drugs and medical preparations. The terminology of this new edition has been made to conform with the "Standard Nomenclature of Diseases and Operations" of the American Medical Association. This dictionary is remarkable for its system of condensation, resulting in the production of a volume of handy size.

A Manual of Physical Therapy. By Richard Kovács, M.D., professor of physical therapy, New York Polyclinic Medical School and Hospital, attending physical therapist, Manhattan State, Harlem Valley State, Columbus and West Side hospitals, visiting physical therapist, New York City Department of Correction Hospitals, consulting physical therapist, New York Infirmary for Women and Children, and Mary Immaculate Hospital, Jamaica, New York, St. Charles Hospital, Jefferson, Long Island, and Hackensack Hospital, Hackensack, New Jersey. Third edition. 12°, cloth, 309 pp., with 118 illustrations. Philadelphia: Lea and Febiger, 1944. $3.25.

This small manual, originally entitled *Physical Therapy for Nurses*, was renamed after it had been written, amplified and brought up to date to furnish a comprehensive volume from the viewpoint of wartime and postwar physical therapy. It is intended as an aid in elementary training on the subject, as well as a manual for physicians and medical personnel seeking information on physical therapy. The plan of the manual is to proceed from a brief statement of the basis and the evolution of physical therapy to a systematic presentation of the physics, physical and physiologic effects, clinical uses, technic of application, and dangers and contraindications of each of the principal physical treatment methods. The text is divided into the headings of heat and light, electricity, water, and massage and exercise. The last two chapters have to do with physical therapy in institutional practice and physical therapy in war.

Manual of Human Protozoa: With special reference to their detection and identification. By Richard R. Kudo, D.Sc., associate professor of zoology, University of Illinois. 12°, cloth, 125 pp., with 29 illustrations. Springfield, Illinois: Charles C Thomas, 1944. $2.00.

This small manual is designed for class use and is based on the author's laboratory notes that have been used in teaching at the University of Illinois. It is intended as a supplement to the large treatises on protozoology. The book contains only essential information needed as a practical guide in detecting and identifying the human protozoa. A number of original drawings prepared from living specimens and microscopic preparations have been inserted in the text to supplement the descriptions of the various types of protozoa. This small manual should be of service to all those interested in an elementary knowledge of human protozoa.

Freedom from Fear: The interrelation of domestic and international programs. By Louis H. Pink, president of Associated Hospital Service of New York. With a foreword by Owen D. Young. 8°, cloth, 254 pp. New York and London: Harper and Brothers, 1944. $2.50.

The aim of this small book is to emphasize the importance of domestic measures for social security and to show that these measures are inadequate unless they are supplemented by broad, economic security and universal prosperity. Approximately half the text is devoted to the discussion of the various forms of insurance. The book also includes sections on hospitalization, industrial medicine and the cost of medical care, all of which may be of interest to physicians.

NOTICES

SOUTH END MEDICAL CLUB

The eighteenth year of the South End Medical Club will begin on Tuesday, October 17, at 12 noon, at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

Dr. Henry Baker, clinical professor of medicine, Tufts College Medical School, will speak on the subject "Sternal Puncture Therapy."

Physicians are cordially invited to attend.

ANNOUNCEMENT

Dr. C. A. Cheever announces a change of address: from 464 Beacon Street, Boston, to the Alexander Home, 29 First Parish Road, Scituate, Massachusetts.

INTERNSHIPS AND RESIDENCIES AT ST. ELIZABETHS

The Civil Service Commission announces a new examination for rotating internships and psychiatric residencies at St. Elizabeths Hospital, the federal institution for the treatment of mental disorders, in Washington, D. C. The positions pay $2433 a year, including overtime pay.

The internships consist of nine months of rotating service, including medicine, surgery, pediatrics (affiliation), obstetrics (affiliation) and, as conditions permit, psychiatry and laboratory. Applicants must be third-year or fourth-year students in an approved medical school.

The psychiatric residencies consist of nine months in psychiatry. Applicants must have successfully completed their fourth year of study in a medical school and they must have the degree of B.M. or M.D. In addition they must have completed an accredited rotating internship of at least nine months or be serving such internship at the time of making application. Persons who attain eligibility but who are still serving their internship may have their names submitted for appointment but they cannot enter on duty until they have completed their internship.

There are no age limits for this examination and no written test will be given. Applications will be accepted until the needs of the service have been met. Application forms may be secured at first- and second-class post offices, from the commission's regional offices, or direct from the United States Civil Service Commission, Washington 25, D. C.

(*Notices continued on page xxi*)